Guo 09/645,37

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(FILE 'MEDLINE, HCAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 15:00:18 ON 20 FEB 2002)

L25 63 DUP REM L24 (61 DUPLICATES REMOVED)

=> d que 125

L1 72 SEA FEASTER ?/AU
L2 8547 SEA SOFIAN ?/AU
L3 3 SEA DOCTOR B/AU
L4 96 SEA (L1 OR L2 OR L3)
L7 19 SEA L4 AND (ACTIVITY OR CONCENTRATION?)(5A) CHOLINESTERASE?)
L8 19099 SEA (ACTIVITY OR CONCENTRATION?)(5A) CHOLINESTERASE?
L9 14 SEA L8 AND (DIFFERENTIAL(5A) (ASSAY? OR MEASUR? OR DETECT?))
L10 45 SEA L8 (5A) DIFFERENTIAL?
L11 20 SEA L10 AND INHIBIT?
L12 SEA L8 AND (STANDARD(2A) CURVE?)
L13 1613 SEA (ASSAY? OR MEASUR? OR DETECT?)(5A) L8
L14 298 SEA L13 AND INHIBITOR?
L15 SEA L14 AND KINETIC?
L16 4 SEA L13 AND INHIBIT?(5A) INTERFER?
L17 SEA L13 AND (COMPETIT?(5A) ENZYM?)
L18 8 SEA L13(5A) SAMPLE?
L19 42 SEA L18 AND INHIBIT?
L20 111 SEA L7 OR L9 OR L11 OR L12 OR (L15 OR L16 OR L17) OR L19
L22 114 SEA L20 NOT PY>2000
L23 92 SEA L7 OR L9 OR L11 OR L12 OR (L15 OR L16 OR L17)
L24 124 SEA L22 OR L23
L25 63 DUP REM L24 (61 DUPLICATES REMOVED)

=> d ibib abs 125 1-63

DUPLICATE 1

L25 ANSWER 1 OF 63 MEDLINE

ACCESSION NUMBER: 2002124614 MEDLINE

DOCUMENT NUMBER: 21821994 PubMed ID: 11831902

TITLE: Carbaphens: binary pyridostigmine-aprophen prodrugs with differential inhibition of acetylcholinesterase, butyrylcholinesterase, and muscarinic receptors.

AUTHOR: Leader Haim; Wolfe Alan David; Chiang Peter K; **Gordon Richard K**

CORPORATE SOURCE: Division of Biochemistry, Walter Reed Army Institute of Research, 503 Robert Grant Road, Silver Spring, MD 20910-7500, USA.

SOURCE: JOURNAL OF MEDICINAL CHEMISTRY, (2002 Feb 14) 45 (4) 902-10.
Journal code: 9716531. ISSN: 0022-2623.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200203

ENTRY DATE: Entered STN: 20020226
Last Updated on STN: 20020308
Entered Medline: 20020307

AB A series of "binary prodrugs" called carbaphens, (1) carbamylated derivatives of one or both of the aromatic rings of the muscarinic receptor antagonist aprophen [(N,N-diethylamino)ethyl 2,2-diphenylpropionate], were synthesized to develop binary prophylactic

Search completed by David Schreiber 308-4292

agents against organophosphorus intoxication. As a group, the carbaphens retained the muscarinic receptor antagonist properties of aprophen but also preferentially inhibited butyrylcholinesterase (BChE) in contrast to acetylcholinesterase (AChE). Therefore, a new series of compounds named pyridophens were designed and synthesized to achieve binary prodrugs to preferentially inhibit AChE over BChE, while still retaining the muscarinic receptor antagonism of aprophen. The pyridophens consist of the basic pyridostigmine skeleton combined with the 2,2-diphenylpropionate portion of aprophen by replacement of the diethylamino group. Three compounds, 9 (a tertiary pyridine), 1? (a quaternary pyridine, and 12 (a tertiary tetrahydropyridine), were found to be effective inhibitors of both BChE and AChE. However, 1?, N-methyl-3-[[(dimethylamino)carbonyl]oxy]-?-(2'2'-diphenylpropionoxy-methyl pyridinium iodide, inhibited AChE selectively over BChE, with a bimolecular rate constant similar to pyridostigmine. In contrast to their potent **cholinesterase** inhibitory **activity**, all of the pyridophen analogues were less potent antagonists of the muscarinic receptor than aprophen.

L25 ANSWER 2 OF 63 BIOSIS COPYRIGHT 2??? BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2001:28???? BIOSIS

DOCUMENT NUMBER: PREV2001?1??89??

TITLE: Acetylcholinesterase characteristics in Caco-2 cells.

AUTHOR(S): Shiu, Kenneth Anthony (1); Pauletti, Giovanni (1); Plageman, Lauren (1)

CORPORATE SOURCE: (1) University of Cincinnati, 3??? Eden Ave., Cincinnati, OH, 452?? USA

SOURCE: FASEB Journal, (March 7, 2001) Vol. 15, No. 4, pp. A557. print.
Meeting Info.: Annual Meeting of the Federation of American Societies for Experimental Biology on Experimental Biology 2001 Orlando, Florida, USA March 31-April 04, 2001
ISSN: 0?9?-663?.

DOCUMENT TYPE: Conference

LANGUAGE: English

SUMMARY LANGUAGE: English

AB The molecular forms, solubility, and subcellular localization of cholinesterases in cultured Caco-2 cells were examined preliminary to determining possible alternative functions of the protein. Caco-2 cells were grown in monolayer and used between passages 5? and 62. Cholinesterase was solubilized with and without detergents and molecular forms were separated on linear sucrose density gradients. Enzyme activity was estimated with a spectrophotometric assay. The cholinesterase exhibited greater activity on acetyl esters and less activity on propionyl and butyryl esters. The enzyme was **inhibited** by BW284c51 and not iso-OMPA and was **inhibited** by substrate concentration in excess of 1? mM. These results established that the principal **cholinesterase** present was acetylcholinesterase (AChE). AChE **activity** increased as **differentiation** progressed from day 3 through day 21. More than ?0% of the AChE required detergent for solubilization. AChE was present primarily as the globular monomer and virtually all of the AChE in intact cells was **inhibited** by echothiophate added to the culture medium. AChE solubilized with Brij-96 sedimented on density gradients at a slower rate than AChE solubilized with Triton X-100. These results suggest that AChE in Caco-2 cells is a membrane bound amphiphilic monomer, with the catalytic site facing outward from the cell.

L2? ANSWER 3 OF 63 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:8?5?18 HCAPLUS

Gu[illegible]

DOCUMENT NUMBER: 136:[illegible]
TITLE: OP nerve agent decontamination, detoxification, and detection using polyurethane immobilized enzymes
AUTHOR(S): **Gordon, Richard K.**; Gunduz, Alper; **Doctor, Bhupendra P.**; Skvorak, John P.; Maxwell, Donald M.; Ross, Michelle; Lenz, David
CORPORATE SOURCE: Division of Biochemistry, Walter Reed Army Institute of Research, Silver Spring, MD, 20910-750[illegible], USA
SOURCE: [illegible]MTS III: An Exploration of Present Capabilities and Future Requirements for Chemical and Biological Medical Treatment, Proceedings of the Chemical and Biological Medical Treatment Symposium, 3rd, Spiez, Switzerland, May 7-12, 2000 (2001), Meeting Date 2000, 78 [illegible]. National Technical Information Service: Springfield, Va.
CODEN: [illegible]
DOCUMENT TYPE: Conference
LANGUAGE: English

AB As an extension of the bioscavenger approach to the protection against organophosphate toxicity, we developed a sponge product, composed of polyurethane immobilized ChEs (AChE and BChE) and organophosphate hydrolases, and oxime for decontaminating organophosphorus nerve agents (OPs) from sensitive biol. surfaces. The ChE-sponge is also a biosensor for OPs so troops can rapidly det. OP exposure and contamination. The enzyme products exhibit remarkable mech. and chem. stability when immobilized and do not leach from the synthesized matrix, yet retain the function of their sol. counterparts. For example, diisopropylfluorophosphate and 7-(methylethoxyphosphinyloxy)-1-methylquinolinium iodide reacted with the immobilized ChEs, and rinsing the sponge with HI-6 restores **cholinesterase activity**, permitting the AChE-sponge to be recycled many times. Since OPs need to be wiped into the sponge to be detoxified, several sponge formulations have been developed to rapidly remove soman from guinea pig skin. Using this enzyme-sponge technol., we are developing a rapid and simple kit to detect OP contamination on humans, in water or almost any environment. ChEs and non-ChE enzymes have been immobilized to yield small OP sensitive and selective biosensors. For long-term OP detection, ChE-biosensors were continuously exposed to untreated natural fresh or salt water over 60 days at room temp. and the badges retained [illegible] of their original activity. In conclusion, immobilized ChEs retain high activity and increased stability, making them suitable for a variety of detoxification and decontamination schemes for both chem. weapons and pesticides directed against ChEs, and as biosensor badges to immediately detect or monitor long-term OP contamination, for example in drinking water.

REFERENCE COUNT: 1[illegible] THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 4 OF 63 MEDLINE
ACCESSION NUMBER: 20[illegible] MEDLINE
DOCUMENT NUMBER: [illegible] PubMed ID: 11801139
TITLE: Acetylcholinesterase assay for cerebrospinal fluid using bupivacaine to inhibit butyrylcholinesterase.
AUTHOR: Klinge[illegible] Klus[illegible] H H; Bauer H T; Pietsch S; Anders J; Venbrocks R A
CORPORATE SOURCE: Clinic of Orthopedics, Rudolf Elle Hospital Eisenberg, Friedrich-Schiller-University Jena, Germany.. [illegible]@aol.com
SOURCE: BMC Biochem, (2001) 2 (1) 17. Journal code: 101084098. ISSN: 1471-2091.

Search completed by David Schreiber 308-4292

Gu [illegible], X.

PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200301
ENTRY DATE: Entered STN: 20021130
Last Updated on STN: 20030105
Entered Medline: 21[illegible]03

AB BACKGROUND: Most test systems for acetylcholinesterase activity (E.C.3.1.1.7.) are using toxic inhibitors (BW284c51 and iso-OMPA) to distinguish the enzyme from butyrylcholinesterase (E.C.3.1.1.8.) which occurs simultaneously in the cerebrospinal fluid. Applying Ellman's colorimetric method, we were looking for a non-toxic inhibitor to restrain butyrylcholinesterase activity. Based on results of previous in vitro studies bupivacaine emerged to be a suitable inhibitor. RESULTS: Pharmacokinetic investigations with purified cholinesterases have shown maximum **inhibition** of butyrylcholinesterase activity and minimal **interference** with acetylcholinesterase activity at bupivacaine final concentrations between 0.1 and 0.5 mmol/l. Based on detailed analysis of pharmacokinetic data we developed three equations representing enzyme inhibition at bupivacaine concentrations of 0.1, 0.2 and 0.5 mmol/l. These equations allow us to calculate the acetylcholinesterase **activity** in solutions containing both **cholinesterases** utilizing the extinction differences **measured** spectrophotometrically in samples with and without bupivacaine. The accuracy of the bupivacaine-inhibition test could be confirmed by investigations on solutions of pure purified cholinesterases and on samples of human cerebrospinal fluid. If butyrylcholinesterase activity has to be assessed simultaneously an independent test using butyrylthiocholine iodide as substrate (final concentration 5 mmol/l) has to be conducted. CONCLUSIONS: The bupivacaine-inhibition test is a reliable method using spectrophotometrical techniques to measure acetylcholinesterase activity in cerebrospinal fluid. It avoids the use of toxic inhibitors for differentiation of acetylcholinesterase from butyrylcholinesterase in fluids containing both enzymes. Our investigations suggest that bupivacaine concentrations of 0.1, 0.2 or 0.5 mmol/l can be applied with the same effect using 1 mmol/l acetylthiocholine iodide as substrate.

ACCESSION NUMBER: 2002:[illegible] BIOSIS
DOCUMENT NUMBER: PREV[illegible]97601
TITLE: Acetylcholinesterase assay for cerebrospinal fluid using bupivacaine to inhibit butyrylcholinesterase.
AUTHOR(S): Pluge, Wolfram H. [1]; Kluge, Harald H.; Bauer, Heike I.; Fritsch, Stefan; Anders, Jens; Vennbocks, Rudolf A.
CORPORATE SOURCE: [1] Klinik f[illegible] Orthopedics, "Rudolf Elle", Hospital Eisenberg, Friedrich-Schiller-University, Jena: wolfpluge@aol.com, kluge@landgraf.med.uni-jena.de, h.bauer@emrz.uni-jena.de, st.pie@gmx.de, [illegible]@web-online.de, jve@rz.uni-jena.de Germany
SOURCE: BMC Biochemistry, December 21, 2001) Vol. 2, No. 17 Cited Apr. 23, 2002, pp. 1-8. http://www.biomedcentral.com/conte nt/pdf/1472-2091-2-17.pdf cited July 2, 2002 http://www.biomedcentral.com/1472-2091. online.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Background: Most test systems for acetylcholinesterase activity (E.C.3.1.1.7.) are using toxic inhibitors (BW284c51 and iso-OMPA) to

Search completed by David Schreiber [illegible]6-4292

distinguish the enzyme from butyrylcholinesterase (E.C.3.1.1.8.) which occurs simultaneously in the cerebrospinal fluid. Applying Ellman's colorimetric method, we were looking for a non-toxic inhibitor to restrain butyrylcholinesterase activity. Based on results of previous in vitro studies bupivacaine emerged to be a suitable inhibitor. Results: Pharmacokinetic investigations with purified cholinesterases have shown maximum **inhibition** of butyrylcholinesterase activity and minimal **interference** with acetylcholinesterase activity at bupivacaine final concentrations between 0.1 and 0.5 mmol/l. Based on detailed analysis of pharmacokinetic data we developed three equations representing enzyme inhibition at bupivacaine concentrations of 0.1, 0.2 and 0.5 mmol/l. These equations allow us to calculate the acetylcholinesterase **activity** in solutions containing both **cholinesterases** utilizing the extinction differences **measured** spectrophotometrically in samples with and without bupivacaine. The accuracy of the bupivacaine-inhibition test could be confirmed by investigations on solutions of both purified cholinesterase activity samples of human cerebrospinal fluid. If butyrylcholinesterase activity has to be assessed simultaneously an independent test using butyrylthiocholine iodide as substrate (final concentration 5 mmol/l) has to be conducted. Conclusions: The bupivacaine-inhibition test is a reliable method using spectrophotometric techniques to measure acetylcholinesterase activity in cerebrospinal fluid. It avoids the use of toxic inhibitors for differentiation of acetylcholinesterase from butyrylcholinesterase in fluids containing both enzymes. Our investigations suggest that bupivacaine concentrations of 0.1, 0.2 or 0.5 mmol/l can be applied with the same effect using 1 mmol/l acetylthiocholine iodide as substrate.

L25 ANSWER 6 OF 63 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2003:[illegible] HCAPLUS
DOCUMENT NUMBER: 138:[illegible]
TITLE: Acetylcholinesterase assay for cerebrospinal fluid using bupivacaine to inhibit butyrylcholinesterase
AUTHOR(S): Plaga, Wolfram H.; Bauer, Heike I.; Bretton, Stefan; Anders, Jens; Venbrocks, Rudolf A.
CORPORATE SOURCE: Clinic of Orthopedics, Rudolf Elle Hospital Eisenberg, Friedrich-Schiller-University Jena, Germany
SOURCE: BMC Biochemistry [Online Computer File] (2001), 2, No pp. given
CODEN: BBMIF2
URL: http://www.biomedcentral.com/1471-2091/2/17
PUBLISHER: BioMed Central Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Background: Most test systems for acetylcholinesterase activity (E.C.3.1.1.7.) are using quite **inhibitors** like BW284c51 and iso-OMPA) to distinguish the enzyme from butyrylcholinesterase (E.C.3.1.1.8.) which occurs simultaneously in the cerebrospinal fluid. Applying Ellman's colorimetric method, we were looking for a non-toxic **inhibitor** to restrain butyrylcholinesterase activity. Based on results of previous in vitro studies bupivacaine emerged to be a suitable **inhibitor**. Results: Pharmacokinetic investigations with purified cholinesterases have shown max. **inhibition** of butyrylcholinesterase activity and minimal **interference** with acetylcholinesterase activity at bupivacaine final concns. between 0.1 and 0.5 mmol/l. Based on detailed anal. of pharmacokinetic data we developed three equations representing enzyme inhibition at bupivacaine concns. of 0.1, 0.2 and 0.5 mmol/l. These equations allow us to calc. the

Search completed by David Schreiber [illegible]508-4292

acetylcholinesterase **activity** in solns. contg. both **cholinesterases** utilizing the extinction differences **measured** spectrophotometrically in samples with and without bupivacaine. The accuracy of the bupivacaine-inhibition test could be confirmed by investigations on solns. of both purified cholinesterase on samples of human cerebrospinal fluid. If butyrylcholinesterase activity has to be assessed simultaneously an independent test using butyrylthiocholine iodide as substrate (final concn. 5 mmol/l) has to be conducted. Conclusions: The bupivacaine-inhibition test is a reliable method using spectrophotometrical techniques to measure acetylcholinesterase activity in cerebrospinal fluid. It avoids the use of toxic **inhibitors** for differentiation of acetylcholinesterase from butyrylcholinesterase in fluids contg. both enzymes. Our investigations suggest that bupivacaine concns. of 0.1, 0.2 or 0.5 mmol/l can be applied with the same effect using 1 mmol/l acetylthiocholine iodide as substrate.

REFERENCE COUNT: [illegible] THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

DUPLICATE 2

L25 ANSWER 7 OF 63 MEDLINE
ACCESSION NUMBER: 2000611:79 MEDLINE
DOCUMENT NUMBER: 20013175 PubMed ID: 10944054
TITLE: Neuronal differentiation in PC12 cells is **inhibited** by chlorpyrifos and its metabolites: is acetylcholinesterase **inhibition** the site of action?.

AUTHOR: Das K P; Barone S Jr
CORPORATE SOURCE: Cell Biology and Molecular Toxicology Branch, U.S. Environmental Protection Agency, Research Triangle Park, North Carolina, 27711, USA.

SOURCE: TOXICOLOGY AND APPLIED PHARMACOLOGY, (1999 Nov 1) 160 (3) 217-30.
Journal code: 0416575. ISSN: 0041-008X.

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199911
ENTRY DATE: Entered STN: 20000119
Last Updated in STN: 20000119
Entered Medline: 19991119

AB Developmental expression of AChE has been associated with neuronal differentiation. [P. G. Layer and E. Willbold, Prog. Histochem. Cytochem. 29, 1-94, 1995]. In this study we used pheochromocytoma (PC12) cells, a noncholinergic cell line, rich in acetylcholinesterase (AChE) **activity**, to examine the effects of **cholinesterase-inhibiting** pesticides on neural **differentiation**. The experimental paradigm was focused on whether alterations in cholinesterase (ChE) activity by a pesticide or its metabolites would affect neurite outgrowth, a morphological marker of neuronal differentiation. Results indicated that (1) in contrast, both total ChE and AChE activities were significantly increased in NGF-primed PC12 cells compared to NGF-unprimed cells, while the basal expression of butyrylcholinesterase (BuChE) activity was much lower (1.3-1% of total ChE activity) in either the presence or the absence of NGF; (2) an increase in AChE activity was highly correlated [r(2) = (.99)] with the extension of neurite outgrowth, suggesting a link between the expression of AChE activity and the elaboration of neurite outgrowth; (3) NGF increased neurite outgrowth in a time- and concentration-dependent manner; and (4) either chlorpyrifos

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(CPF) or its metabolites (CPF oxon and TCP) **inhibited** NGF-induced neurite outgrowth (branches per cell, fragments per cell, total neurite outgrowth per cell) in PC12 cells. These data suggest that the expression of AChE activity is associated with the extension of neurite outgrowth. Both enzyme activity and neurite branching were disrupted by CPF oxon; however, CPF and its other metabolite TCP (1 microgram/ml) caused **inhibition** of neurite outgrowth in the absence of ChE **inhibition**, suggesting an alternative mechanism(s) may be involved in pesticide-induced **inhibition** of differentiation.

L25 ANSWER 8 OF 63 MEDLINE

ACCESSION NUMBER:	1999273286 MEDLINE
DOCUMENT NUMBER:	99273286 PubMed ID: 10341740
TITLE:	Oral and dermal absorption of chlorpyrifos: a human volunteer study.
AUTHOR:	Griffin P; Mason H; Heywood K; Cocker J
CORPORATE SOURCE:	Health and Safety Laboratory, Sheffield, UK.
SOURCE:	OCCUPATIONAL AND ENVIRONMENTAL MEDICINE, (1999 Jan) 56 (1) 10-3. Journal code: 9422759. ISSN: 1351-0711.
PUB. COUNTRY:	ENGLAND: United Kingdom
DOCUMENT TYPE:	Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:	English
FILE SEGMENT:	Priority Journals
ENTRY MONTH:	199905
ENTRY DATE:	Entered STN: 19990607 Last Updated on STN: 19990607 Entered Medline: 19990527

AB OBJECTIVES: To determine the **kinetics** of elimination of urinary dialkylphosphate metabolites after oral and dermally applied doses of the organophosphate pesticide chlorpyrifos to human volunteers and to determine whether these doses affected plasma and erythrocyte cholinesterase activity. METHODS: Five volunteers ingested 1 mg (2852 nmol) of chlorpyrifos. Blood samples were taken over 24 hours and total void volumes of urine were collected over 100 hours. Four weeks later 28.59 mg (81567 nmol) of chlorpyrifos was administered dermally to each volunteer for 8 hours. Unabsorbed chlorpyrifos was washed from the skin and retained for subsequent measurement. The same blood and urine sampling regime was followed as for the oral administration. Plasma and erythrocyte cholinesterase concentrations were determined for each blood sample. The concentration of two urinary metabolites of chlorpyrifos--diethylphosphate and diethyl-thiophosphate--was determined for each urine sample. RESULTS: The apparent elimination half life of urinary dialkylphosphates after the oral dose was 15.5 hours and after the dermal dose it was 30 hours. Most of the oral dose (mean (range) 93% (55-115%)) and 1% of the applied dermal dose was recovered as urinary metabolites. About half (53%) of the dermal dose was recovered from the skin surface. The absorption rate through the skin, as measured by urinary metabolites was 456 ng/cm2/h. Blood plasma and erythrocyte cholinesterase activity did not fall significantly during either dosing regime. CONCLUSION: An oral dose of chlorpyrifos was readily absorbed through the skin and almost all of the dose was recovered as urinary dialkylphosphate metabolites. Excretion was delayed compared with the oral dose. Only a small proportion of the applied dose was recovered during the course of the experiment. The best time to collect urine samples for biological monitoring after dermal exposure is before the shift the next day. The amount of chlorpyrifos used did not depress acetyl **cholinesterase activity** but could be readily **detected** as urinary dialkylphosphate metabolites indicating that

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the primary assay is a more sensitive indicator of exposure.

L25 ANSWER 9 OF 63 SCISEARCH COPYRIGHT 2003 ISI (R)
ACCESSION NUMBER: 1998:330832 SCISEARCH
THE GENUINE ARTICLE: ZJ036
TITLE: Stable complexes involving acetylcholinesterase and amyloid-beta peptide change the biochemical properties of the enzyme and increase the neurotoxicity of Alzheimer's fibrils
AUTHOR: Alvarez A; Alarcon R; Opazo C; Campos E O; Munoz F J; Calderon F H; Dajas F; Gentry M K; **Doctor B P**; Dellepiane M G; Inestrosa N C (Reprint)
CORPORATE SOURCE: CATHOLIC UNIV CHILE, MOL NEUROBIOL UNIT, POB 114-D, SANTIAGO, CHILE (Reprint); PONTIFICIA UNIV CATOLICA CHILE, FAC CIENCIAS BIOL, DEPT BIOL CELULAR & MOL, SANTIAGO, CHILE; INST INVEST BIOL CLEMENTE ESTABLE, DEV NEUROQUIM, MONTEVIDEO, URUGUAY; WALTER REED ARMY MED CTR, WALTER REED ARMY INST RES, DIV BIOCHEM, WASHINGTON, DC 20307; UNIV FED RJ DE JANEIRO, INST BIOFIS, RIO JANEIRO, BRAZIL
COUNTRY OF AUTHOR: CHILE; URUGUAY; USA; BRAZIL
SOURCE: JOURNAL OF NEUROSCIENCE, (1 MAY 1998) Vol. 18, No. 9, pp. 3211-3223.
Publisher: SOC NEUROSCIENCE, 11 DUPONT CIRCLE, NW, STE 500, WASHINGTON, DC 20036.
ISSN: 0270-6474.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 39
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

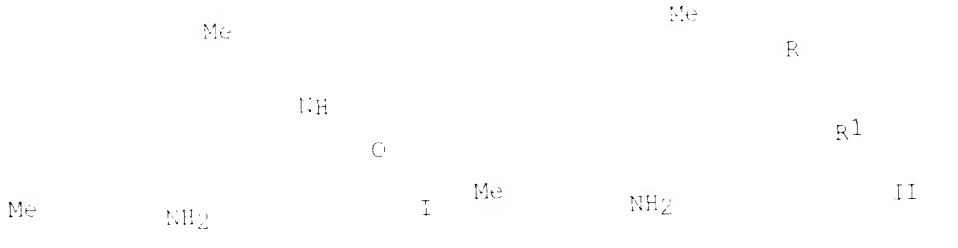
AB Brain acetylcholinesterase (AChE) forms stable complexes with amyloid-beta peptide (A beta) during its assembly into filaments, in agreement with its colocalization with the A beta deposits in Alzheimer's brain. The association of the enzyme with nascent A beta aggregates occurs as early as after 30 min of incubation. Analysis of the catalytic activity of the AChE incorporated into these complexes shows an anomalous behavior reminiscent of the AChE associated with senile plaques, which includes a resistance to low pH, high substrate concentrations, and lower sensitivity to AChE inhibitors. Furthermore, the toxicity of the AChE-amyloid complexes is higher than that of the A beta aggregates alone. Thus, in addition to its possible role as a heterogeneous nucleator during amyloid formation, AChE, by forming such stable complexes, may increase the neurotoxicity of A beta fibrils and thus may determine the selective neuronal loss observed in Alzheimer's brain.

L25 ANSWER 10 OF 63 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:470878 HCAPLUS
DOCUMENT NUMBER: 129:121494
TITLE: Synthesis and anticholinesterase activity of huperzine A analogs containing phenol and pyrocatechol replacements for the pyridone ring
AUTHOR(S): Campiani, Giuseppe; Kozikowski, Alan P.; Wang, Shaomeng; Ming, Liu; Nacci, Vito; Saxena, Ashima; **Doctor, Bhupendra P.**
CORPORATE SOURCE: Dipartimento Farmaco Chimico Tecnologico, Siena University, Siena, 53100, Italy
SOURCE: Bioorganic & Medicina. Chemistry Letters (1998), 8(11), 1413-1418
CODEN: BMCLE8; ISSN: 0960-894X

Search completed by David Schreiber 306-4292

Sep. 08/04, [illegible]

PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



AB Based upon modeling results obtained using the crystal structure of huperzine A (I) in complex with acetylcholinesterase (AChE), two novel analogs of this potent AChE inhibitor (II; R = H, R1 = OH; R = R1 = OH) were designed with phenol or pyrocatechol rings replacing the pyridone ring. From the modeling studies, the pyrocatechol analog appeared capable of replacing one of the crystallog. waters bridging huperzine with Tyr 130 and Glu 199 of AChE. The synthesis of these materials by use of a palladium catalyzed biscycloannulation strategy is detailed together with the results of AChE inhibition assays.

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 11 OF 63 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:262348 HCAPLUS
DOCUMENT NUMBER: 132:13479
TITLE: Cholinesterases and agriculture: Humans, laboratory animals, wildlife
AUTHOR(S): Watson, R. W.; McCurdy, S. A.; Henderson, C. D.; McCarthy, S. A.; Billitti, J. E.
CORPORATE SOURCE: University of California, Davis, Davis, CA, 95616, USA
SOURCE: Structure and Function of Cholinesterases and Related Proteins, [International Meeting on Cholinesterases and Related Proteins], 6th, La Jolla, CA, Mar. 20-24, 1999 (1999), 535-546. Editor(s): **Doctor, Bhupendra P.** Plenum Publishing Corp.: New York, N. Y.
CODEN: 69VDAY
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English

AB A review with 21 refs. Widespread use of organophosphate and carbamate esters as pesticides in agriculture and stockpiling them as chem. warfare agents require the means of detection of their residues and recognition of their effects. The toxicity of these chems. is a result of inhibition of the cholinesterase (ChE). Measurements of the ChE activity in blood and other tissues of humans, lab. animals, and wildlife are used to assess exposures, effects and risks of these agents. The emphasis in this report is on the assay that allows to det. the ChE activity using thiocholine, which is hydrolyzed by ChEs, and the released thiol groups react with the chromogen dithiobisnitrobenzoate to produce a yellow color.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

Search completed by David Schreiber 308-4292

Gu. 89/847,

L25 ANSWER 12 OF 63 MEDLINE
ACCESSION NUMBER: 1998436089 MEDLINE
DOCUMENT NUMBER: 98436089 PubMed ID: 9765060
TITLE: Toxicokinetics of soman in cerebrospinal fluid and blood of anaesthetized pigs.
AUTHOR: Goransson-Nyberg A; Fredriksson S A; Karlsson B; Lundstrom M; Cassel G
CORPORATE SOURCE: Defence Research Establishment, Department of Biomedicine, Umea, Sweden.
SOURCE: ARCHIVES OF TOXICOLOGY, (1998 Jul-Aug) 72 (8) 459-67.
Journal code: 0417615. ISSN: 0340-5761.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199812
ENTRY DATE: Entered STN: 19990115
Last Updated on STN: 19990115
Entered Medline: 19981210

AB The toxicokinetics of the four stereoisomers of the nerve agent C(+/-)P(+/-)-soman was analysed in cerebrospinal fluid (CSF) and blood in anaesthetized, spontaneously breathing pigs during a 90-min period after injection of soman. The pigs were challenged with different intravenous (i.v.) doses of C(+/-)P(+/-)-soman corresponding to 0.75-3.0 LD50 (4.5, 9.0 and 18 microg/kg in a bolus injection and 0.45 microg/kg per min as a slow infusion). Artificial ventilatory assistance was given if, after soman intoxication, the respiratory rate decreased below 19 breaths/min. Blood samples were taken from a femoral artery and CSF samples from an intrathecal catheter. The concentrations of the soman isomers were determined by gas chromatography coupled with high resolution mass spectrometry. All four isomers of soman were detected in both blood and CSF samples. The relatively non-toxic C(+/-)P(+) isomers disappeared from the blood stream and CSF within the first minute, whereas the levels of the highly toxic C(+/-)P(-) isomers could be followed for longer, depending on the dose. Concurrently with the soman analyses in blood and CSF, **cholinesterase** (ChE) **activity** and cardiopulmonary parameters were **measured**. C(+/-)P(-) isomers showed approx. 100% bioavailability in CSF when C(+/-)P(+/-)-soman was given i.v. as a bolus injection. In contrast, C(+/-)P(-) isomers displayed only 30% bioavailability in CSF after slow i.v. infusion of soman. The ChE activity in blood decreased below 20% of baseline in all groups of pigs irrespective of the soman dose. The effect of soman intoxication on the respiratory rate, however, seems to be dose-dependent and the reason for ventilatory failure and death. Artificial ventilation resulted in survival of the pigs for the time-period studied.

DUPLICATE 3

L25 ANSWER 13 OF 63 MEDLINE
ACCESSION NUMBER: 1998230152 MEDLINE
DOCUMENT NUMBER: 98230152 PubMed ID: 9570306
TITLE: Poverty, production, and health: **inhibition** of erythrocyte cholinesterase via occupational exposure to organophosphate insecticides in Chiapas, Mexico.
AUTHOR: Tinoco-Ojanguren R; Halperin D C
CORPORATE SOURCE: El Colegio de la Frontera Sur-Ecosur San Cristobal de Las Casas Chiapas, Mexico.
SOURCE: ARCHIVES OF ENVIRONMENTAL HEALTH, (1998 Jan-Feb) 53 (1) 29-35.
Journal code: 0212627. ISSN: 0003-9896.
PUB. COUNTRY: United States

Search completed by David Schreiber 308-4292

Gas Analysis, S

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 1998-05
ENTRY DATE: Entered STN: 19980514
Last Updated on STN: 19980514
Entered Medline: 19980506

AB Occupational exposure to organophosphate pesticides and its effects on the concentration of erythrocyte cholinesterase in the rural population of Chiapas, Mexico, are described. The authors surveyed agricultural production and pesticide use was surveyed among 199 campesinos (peasants) in three communities that used various agricultural production systems. The authors **measured** the **concentration** of the **cholinesterase** enzyme in blood **samples** obtained from 65 campesinos before and after exposure to the insecticide. The authors established a comparison value for the population that was not exposed occupationally. The exposure values of the enzyme concentration were significantly lower than preexposure values ($p = .0001$) and reference group values ($p = .0008$). Individuals in the community characterized by subsistence production had significantly lower levels of the enzyme than individuals in the other two communities ($p = .01$). This result suggested that a greater risk of adverse health effects existed among the poorest communities.

L25 ANSWER 14 OF 63 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:204765 HCAPLUS
DOCUMENT NUMBER: 126:143678
TITLE: **Inhibition** of **interfering** endogenous enzyme activity in assays of biological fluids
INVENTOR(S): White, Mark D.; Law, Wai T.
PATENT ASSIGNEE(S): Actimed Laboratories, Inc., USA
SOURCE: U.S., 12 pp., Cont.-in-part of U.S.Ser. No. 828,453, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5610025	A	1997[illegible]	US 1995-[illegible]	19950710
AT 151466	E	1997[illegible]	AT 1995-[illegible]	19950128
CA 2129117	[illegible]	1996[illegible]	CA 1995-2129117	19950128
			US 1992-828453	19920131

PRIORITY APPLN. INFO.:
AB The invention describes biol. assays in which hydrogen peroxide is used as an oxidizing agent, or wherein hydrogen peroxide is used to oxidize a dye or other intermediate to generate a detectable species. The stability of the hydrogen peroxide in the presence of at least one other enzyme which decomps. hydrogen peroxide, e.g., catalase, is enhanced by the addn. of a suitable inhibitor for the enzyme and the inhibitor does not substantially inhibit enzymes used in the assay. When catalase is the enzyme to be inhibited, catalase inhibitors that can be used in the biol. systems include hydroxylamine sulfate. The enzyme inhibitor can be incorporated in an integral anal. device such as for cholesterol detn. in blood. Other analytes are triglycerides, glucose, HDL, LDL, uric acid, lactic acid, [illegible] type fatty acids, etc.

Search completed by David Schreiber 308-4292

L25 ANSWER 15 OF [illegible] HCAPLUS COPYRIGHT 2[illegible] ACS
ACCESSION NUMBER: 1997:720388 HCAPLUS
DOCUMENT NUMBER: 127:325213
TITLE: Differences in Active Site Gorge Dimensions of Cholinesterases Revealed by Binding of Inhibitors to Human Butyrylcholinesterase
AUTHOR(S): Saxena, Ashima; Redman, Ann M. G.; Jiang, Xuliang; Lockridge, Oksana; **Doctor, B. P.**
CORPORATE SOURCE: Division of Biochemistry, Walter Reed Army Institute of Research, Washington, DC, 20307, USA
SOURCE: Biochemistry (1997), 36(48), 14642-14651
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Amino acid sequence alignments of cholinesterases revealed that 6 of 14 aromatic amino acid residues lining the active center gorge of acetylcholinesterase are replaced by aliphatic amino acid residues in butyrylcholinesterase. The Y337 (F330), in mammalian acetylcholinesterase, which is replaced by A328 in human butyrylcholinesterase, is implicated in the binding of ligands such as huperzine A, edrophonium, and acridines and one end of bisquaternary congeners, such as BW284C51 and decamethonium. Y337 may sterically hinder the binding of phenothiazines such as ethopropazine, which contains a bulky exocyclic substitution. Inhibition studies of (-)-huperzine A with human butyrylcholinesterase mutants, where A328 (KI = 194.6 .mu.M) was modified to either F (KI = 0.6 .mu.M, as in Torpedo acetylcholinesterase) or Y (KI = 0.032 .mu.M, as in mammalian acetylcholinesterase), confirmed previous observations made with acetylcholinesterase mutants that this residue is important for binding huperzine A. Inhibition studies of ethopropazine with butyrylcholinesterase mutants, where A328 (KI = 0.18 .mu.M) was modified to either F (KI = 0.62 .mu.M) or Y (KI = 0.08 .mu.M), suggested that A328 was not solely responsible for the selectivity of ethopropazine. Vol. calcns. for the active site gorge showed that the poor inhibitory activity of ethopropazine toward acetylcholinesterase was due to the smaller dimension of the active site gorge, which was unable to accommodate the bulky inhibitor mol. The vol. of the butyrylcholinesterase active site gorge is .apprx.200 .ANG.3 larger than that of the acetylcholinesterase gorge, which allows the accommodation of ethopropazine in two different orientations as demonstrated by rigid-body refinement and mol. dynamics calcns.

DUPLICATE 4

L25 ANSWER 16 OF 63 MEDLINE
ACCESSION NUMBER: 97292515 MEDLINE
DOCUMENT NUMBER: 97292515 PubMed ID: 9147776
TITLE: Mipafox **differential** inhibition **assay** for heart muscle cholinesterases: substrate specificity and inhibition of three isoenzymes by physostigmine and quinidine.
AUTHOR: Brammilius J M; Hasselmeyer K H; Gorska B D; Kreutner H; Zech K
CORPORATE SOURCE: Department of Cardiology, Georg-August University, Gottingen, Germany.
SOURCE: GENERAL PHARMACOLOGY, (1997 Apr) 28 (4) 567-75.
Journal code: 7602417. ISSN: 0306-3623.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals

Search completed by David Schreiber 308-4292

Gar Cra-4r, S

ENTRY MONTH: 199708

ENTRY DATE: Entered STN: 19970825

Last Updated on STN: 19970825

Entered Medline: 19970811

AB 1. A **differential** inhibition **assay** was developed for the quantitative determination of cholinesterase isoenzymes acetylcholinesterase (AChE; EC 3.1.1.7), cholinesterase (BChE; EC 3.1.1.8), and atypical cholinesterase in small samples of left ventricular porcine heart muscle. 2. The assay is based on kinetic analysis of irreversible cholinesterase inhibition by the organophosphorus compound N,N'-di-isopropylphosphorodiamidic fluoride (mipafox). With acetylthiocholine (ASCh as substrate (1.25 mM), hydrolytic **activities** (A) of **cholinesterase** isoenzymes were determined after preincubation (60 min, 25 degrees C) of heart muscle samples with either saline total activity, A tau), 7 microM mipafox AM1), or 0.8 mM mipafox (AM2): (BChE) = A tau-AM1, (AChE) = AM1-AM2, (Atypical ChE) = AM2. 3. The mipafox **differential** inhibition **assay** was used to determine the substrate hydrolysis patterns of myocardial cholinesterases with ASCh, acetyl-beta-methylthiocholine (A beta MSCh), propionylthiocholine (PSCh), and butyrylthiocholine (BSCh). The substrate specificities of myocardial AChE and BChE resemble those of erythrocyte AChE and serum BChE, respectively. Michaelis constants KM with ASCh were determined to be 0.15 mM for AChE and 1.4 mM for BChE. 4. Atypical cholinesterase, in respect to both substrate specificity and inhibition kinetics, differs from **cholinesterase activities** of vertebrate tissue and, up to now, could be identified exclusively in heart muscle. The enzyme's Michaelis constant with ASCh was determined to be 4.0 mM. 5. The reversible inhibitory effects of physostigmine (eserine) and quinidine in heart muscle cholinesterases were investigated using the **differential** inhibition **assay**. With all three isoenzymes, the inhibition kinetics of both substances were strictly competitive. The physostigmine inhibition of AChE was most pronounced (Ki = 0.22 microM). Quinidine most potently inhibited myocardial BChE Ki = 35 microM).

L25 ANSWER 17 OF 63 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 5

ACCESSION NUMBER: 1997:91947 HCAPLUS

DOCUMENT NUMBER: 128:111582

TITLE: Heterogeneity of human serum cholinesterase revealed by thiocholine substrates

AUTHOR(S): Simeon-Rudolf, Vera; Kursic, Brigita

CORPORATE SOURCE: Laboratory of Biochemistry, Institute for Medical Research and Occupational Health, Zagreb, HR-10001, Croatia

SOURCE: Periodicum Biologorum (1996), 98(3), 331-336

CODEN: PDBIAD; ISSN: 0031-5362

PUBLISHER: Hrvatsko Prirodoslovno Drustvo

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The activity of human serum cholinesterase (EC 3.1.1.8) was measured with acetylthiocholine (ATCh), propionylthiocholine (PTCh) or butyrylthiocholine (BTCh) in the presence and absence of specific reversible and progressive **inhibitors** and after heat inactivation of the enzyme. Mol. forms of cholinesterase sepd. by electrophoresis on PAA gel were developed by the three substrates. The aim of the study was to show whether the thiocholine substrates were interchangeable for measuring the activity and for visualization of the mol. forms of the enzyme. **Cholinesterase activity** was **measured** with the substrates in the concn. range from 0.01 to 10

Search completed by David Schreiber 308-4292

mM. **Kinetic** parameters were calcd. by a non-linear regression anal. using three equations describing models of substrate hydrolysis. The degree of enzyme inhibition by the three organophosphates VX, iso-OMPA and BNPP, by a reversible **inhibitor** BW284C51 and by heat inactivation at 60 and 61 degree was followed by measuring the remaining activity alternately with the three substrates. Serum was subjected to polyacrylamide homogeneous (7.5%) and d. gradient (4/30%) electrophoresis and serum cholinesterase mol. forms were visualized by the substrates. The band intensities were scanned and the participation of the mol. forms to the total activity was evaluated. Relative mobilities of the mol. forms on gel were compared to the relative mobilities of the std. proteins of known mol. masses. The activities of the enzyme against three substrates deviated from the Michaelis-Menten **kinetics** in a very similar way. The activities fitted reasonably well the equation assuming the binding of an addnl. substrate to the peripheral regulatory site on the enzyme. According to the **kinetic** consts. ATCh was shown to be a less favorable substrate than BTCh or PTCh. On homogeneous gel seven active cholinesterase bands were discernible and on d. gradient gel there were ten. The same pattern of mol. forms was obtained with all the three substrates. Mol. masses were from 102 to 535 kDa. The most active bands were ChE-5 and ChE'-7 on homogeneous and gradient gels resp., contributing about 50% to the total activity. In following heat inactivation of the enzyme and inhibition by progressive **inhibitors** the substrates were completely interchangeable. However, when the activity was measured by ATCh in the presence of a reversible **inhibitor**, a higher degree of inhibition was obtained than with PTCh and BTCh. Also, to develop cholinesterase bands of equal intensity a longer time and/or higher ATCh concn. was needed than of two other substrates.

L25 ANSWER 18 OF 63 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:[illegible] HCAPLUS
DOCUMENT NUMBER: [illegible]
TITLE: Post-exposure treatment of organophosphate poisoning with butyrylcholinesterase in rats
AUTHOR(S): Genovese, Raymond F.; Carranto, German R.; Gordon, Kimberly A.; Morrison, Elaine E.; **Doctor, Bhupendra P.**
CORP. SOURCE: Divisions of Neurosciences and Biochemistry, Walter Reed Army Institute of Research, Washington, DC, [illegible], USA
SOURCE: Medical Defense Bioscience Review, Proceedings, Baltimore, May 12-16, 1996 (1996), Volume 1, 175-182. National Technical Information Service: Springfield, [illegible].
CODEN: 64UTAN
DOCUMENT TYPE: Conference
LANGUAGE: English

AB Effects of the organophosphate chlorpyrifos (CPF) and subsequent administration of equine butyrylcholinesterase (Eq-BChE) were evaluated in rats using operant conditioning and blood **cholinesterase** (ChE) **activity**. Expt. 1 showed that CPF (30 mg/kg, n = 5) produced prolonged behavioral disruption and inhibited blood BChE and AChE activity. Behavioral performance recovered before ChE activity, which was inhibited for at least 10 days. In Expt. 2, CPF administration was followed, four hours later, by 5000 U Eq-BChE (n = 4) or vehicle (n = 4). A third group (n = 2) received 5000 U Eq-BChE only. In both groups receiving CPF, behavior disruption was similar to that seen in Expt. 1, although Eq-BChE - treated rats showed slightly quicker recovery. Dramatic differences in blood ChE activity were obsd. among the three

groups. As expected, rats receiving Eq-BChE only, showed a precipitous rise in BChE activity. Rats receiving CPF and vehicle showed inhibited ChE activity similar to that seen in Expt. 1. In contrast, rats receiving CPF followed by Eq-BChE did not show inhibited BChE activity, and, on av., showed slight increases. BChE activity was, however, far less than that obsd. in rats receiving Eq-BChE only. These results indicate that bioscavenger enzyme was inhibited by residual anticholinesterase activity produced by CPF exposure four hours earlier. Therefore, a post-exposure bioscavenger therapy for OP toxicity is a viable concept.

DUPLICATE 6

L25 ANSWER 19 OF 6[illegible] MEDLINE
ACCESSION NUMBER: 97137647 MEDLINE
DOCUMENT NUMBER: 97137647 PubMed ID: 9082484
TITLE: Amperometric microsensors for monitoring choline in the extracellular fluid of brain.
AUTHOR: Cargill R S; Mignae A C
CORPORATE SOURCE: Department of Chemistry, University of Pittsburgh, PA 15260, USA.
CONTRACT NUMBER: 1R29NS31442 (NINDS)
SOURCE: JOURNAL OF NEUROSCIENCE METHODS, (1996 Dec) 70 (1) 73-82.
Journal code: [illegible]. ISSN: 0165-0270.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199734
ENTRY DATE: Entered STN: [illegible]
Last Updated on STN: 19990[illegible]
Entered Medline: 19970402

AB Selective amperometric enzyme microsensors for monitoring low micromolar concentrations of choline in extracellular fluid of rat brain have been developed. Preparation of the choline microsensors involved the modification of carbon fiber microcylinder electrodes (10 microns diameter, 300-400 microns long) with a cross-linked redox-active gel containing horseradish peroxidase and choline oxidase. Rejection of the noise recorded from the choline microsensors implanted in living brain tissue improved the in vivo detection capabilities of the sensors. The microsensors and a **differential detection** scheme were used to estimate the basal concentration of choline in striatal tissue at 6.0 +/- 2.9 microM and to measure changes in choline concentrations of 6.1 +/- 0.7 microM in vivo. The microsensors were also used to monitor choline produced following the injections of acetylcholine in vivo. Coinjections of neostigmine and acetylcholine significantly lowered the choline response recorded with the microsensors, confirming that the response following the injections of acetylcholine alone was due to the activity of endogenous acetylcholinesterase. Comparison of the maximal rate of decrease in choline concentration following the injections of 1 mM choline and 1 mM acetylcholine was used to estimate the rate of acetylcholine clearance from extracellular fluid through **cholinesterase activity** at approx. 2.5 microM/min.

L25 ANSWER 20 OF 63 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:375214 HCAPLUS
DOCUMENT NUMBER: 125:[illegible]
TITLE: The successful use of oximes in vitro for the differential diagnosis of low levels of cholinesterase activity
AUTHOR(S): Borowiak, K.; Wolski, St; Jarmolowicz, Z.
CORPORATE SOURCE: Departments Forensic Medicine, Pomeranian Academy

Search completed by David Schreiber 308-4292

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Medicine, ..., Pol.

SOURCE: Advances in Forensic Sciences, Proceedings of the Meeting of the International Association of Forensic Sciences, 13th, Duesseldorf, Aug. 22-28, 1993 (1995), Volume 5, 158-161. Editor(s): Jacob, Bernhard; Bonte, Wolfgang. Verlag Dr. Koester: Berlin, Germany.
CODEN: 62SGAS

DOCUMENT TYPE: Conference
LANGUAGE: English

AB The authors demonstrate the possibility of using oximes in vitro for **differentiating** depressed **cholinesterase** **activity** in intoxications with various insecticide **inhibitors** and in the course of hepatic disease.

L25 ANSWER 21 OF 63 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 96120767 MEDLINE
DOCUMENT NUMBER: 96120767 PubMed ID: 8548921
TITLE: Evaluation of the decarbamylation process of **cholinesterase** during **assay** of enzyme **activity**.
AUTHOR: Rotenberg M; Almog S
CORPORATE SOURCE: Institute of Clinical Toxicology and Pharmacology, Sheba Medical Center, Tel Hashomer, Israel.
SOURCE: CLINICA CHIMICA ACTA, (1995 Sep 15) 240 (2) 107-16.
Journal code: 1302422. ISSN: 0009-8981.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199602
ENTRY DATE: Entered STN: 19960306
Last Updated on STN: 19970203
Entered Medline: 19960222

AB The **activity** of carbamylated **cholinesterase** increases continuously during **assay**, suggesting that progressive decarbamylation takes place. The following effects of assay conditions on the observed decarbamylation were studied: the effect of the sulfhydryl group of nitrobenzoate produced in the course of Ellman assay, the effect of substrate and the effect of sample dilution during assay. This study indicates that sample dilution is the main trigger to the decarbamylation observed during **assay** of **cholinesterase** **activity**. The process was described as a first-order reaction during which the inhibited enzyme gives place to the active form. **Kinetic** constants for decarbamylation of human pseudocholinesterase (EC 3.1.1.8) at 30 degrees C were approximately 0.005 min-1 for dimethylcarbamates and 0.010 min-1 for monomethylcarbamates, when 1 mmol/l propionylthiocholine was used as substrate.

L25 ANSWER 22 OF 63 MEDLINE DUPLICATE 8
ACCESSION NUMBER: 95277457 MEDLINE
DOCUMENT NUMBER: 95277457 PubMed ID: 7758210
TITLE: Differentiation between organophosphate and carbamate poisoning.
AUTHOR: Rotenberg M; Shefi M; Dany S; Dore I; Tirosh M; Almog S
CORPORATE SOURCE: Institute of Clinical Toxicology and Pharmacology, Chaim Sheba Medical Center, Tel Hashomer, Israel.
SOURCE: CLINICA CHIMICA ACTA, (1995 Jan 31) 234 (1-2) 11-21.
Journal code: 1302422. ISSN: 0009-8981.
PUB. COUNTRY: Netherlands

Search completed by David Schreiber 308-4292

Guo 09/[illegible],[illegible]

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: [illegible]
ENTRY DATE: Entered STN: 19950707
Last Updated on STN: 19970203
Entered Medline: 19950628

AB We propose a novel and simple assay for the real-time differentiation between carbamate and organophosphate inhibition of cholinesterase, based on our observations of the **kinetic** behavior of inhibited enzyme. The **assay** of carbamylated **cholinesterase** **activity** over time follows a non-linear **kinetic** pattern, whereas that of phosphorylated enzyme activity is linear. This feature can be exploited to differentiate between carbamate and organophosphate cholinesterase inhibition. The non-linear pattern characteristic of carbamates is easily discernible at degrees of inhibition of 40% or more. In this setting, **cholinesterase activity** ought to be **measured** continuously for about 1 h to obtain the **kinetic** pattern of enzyme activity. The initial activity, measured during the first 5 min of assay, represents the activity of enzyme in vivo. In vitro reactivation of inhibited cholinesterase allows the estimation of full potential activity of enzyme prior to poisoning, so that percentage of inhibition can be calculated. Reactivation of carbamylated cholinesterase is obtained by the incubation of diluted enzyme at 37 degrees C for 2.5 h prior to assay, whereas phosphorylated (non-aged) enzyme is reactivated by a 30 min incubation with oximes. In cases of mild exposure to cholinesterase **inhibitors** (< 40% inhibition), the response of enzyme to in vitro reactivation serves as a complementary test for exposure and for the nature of the **inhibitor**. All the results presented in this work refer to plasma cholinesterase. Erythrocyte cholinesterase was found to behave very similarly to plasma enzyme and its results have not been reported here.

L25 ANSWER 23 OF 63 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:[illegible] HCAPLUS
DOCUMENT NUMBER: 122:29044
TITLE: Identification of amino acid residues involved in the binding of Huperzine A to cholinesterases
AUTHOR(S): Saxena, Asmira; Qian, Naifeng; Kovach, Ildiko M.; Kozikowski, A. P.; Pang, Y. P.; Vellom, Daniel C.; Radic, Zoran; Quinn, Daniel; Taylor, Palmer; **Doctor, Bhupendra P.**
CORPORATE SOURCE: Dev. Biochem., Walter Reed Army Inst. Res., Washington, DC, 20307-5100, USA
SOURCE: Protein Science (1994), 3(10), 1770-6
CODEN: PRCIEI; ISSN: 0961-8368
PUBLISHER: Cambridge University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Huperzine A, a potential agent for therapy in Alzheimer's disease and for prophylaxis of organophosphate toxicity, has recently been characterized as a reversible inhibitor of cholinesterases. To examine the specificity of this novel compd. in more detail, the authors have examd. the interaction of the 2 stereoisomers of Huperzine A with cholinesterases and site-specific mutants that detail the involvement of specific amino acid residues. Inhibition of fetal bovine serum acetylcholinesterase by (-)-Huperzine A was 35-fold more potent than (+)-Huperzine A, with KI values of 6.2 nM and 210 nM, resp. In addn., (-)-Huperzine A was 88-fold more potent in inhibiting Torpedo acetylcholinesterase than (+)-Huperzine

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A, with KI values of 2.4 and 22 nM, resp. Far larger KI values that did not differ between the 2 stereoisomers were obsd. with horse and human serum butyrylcholinesterase can be distinguished by the amino acid Tyr, Phe, or Ala in the 332 position, resp. Studies with mouse acetylcholinesterase mutants, Tyr337(330)Phe and Tyr337(330) Ala yielded a difference in reactivity that closely mimicked the native enzymes. In contrast, mutation of the conserved Glu 199 residue to Gln in Torpedo acetylcholinesterase produced only a 3-fold increase in KI value for the binding of Huperzine A. Mol. mechanics energy minimization of the complexes formed between each of the 2 stereoisomers of Huperzine A and fetal bovine serum acetylcholinesterase, Torpedo acetylcholinesterase, or human butyrylcholinesterase also revealed that (-)-Huperzine A gave a better fit than (+)-Huperzine A and implicated Tyr 337(330) in the stereoselectivity of Huperzine A.

L25 ANSWER 24 OF 65 MEDLINE
ACCESSION NUMBER: 94027822 MEDLINE
DOCUMENT NUMBER: 94027822 PubMed ID: 8214574
TITLE: Development and optimization of reactivation techniques for carbamate-inhibited brain and plasma cholinesterases in birds and mammals.
AUTHOR: Hunt K A; Hooper M J
CORPORATE SOURCE: Department of Environmental Toxicology, Clemson University, Pendleton, South Carolina 29670.
SOURCE: ANALYTICAL BI CHEMISTRY, (1993 Aug 1) 212 (2) 335-43.
Journal code: 0370535. ISSN: 0003-2697.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199311
ENTRY DATE: Entered STN: 19940117
Last Updated on STN: 19970206
Entered Medline: 19931116

AB Two biochemical assays were developed which promote and measure the induced reactivation of carbamate-inhibited cholinesterases in avian and mammalian brain and plasma samples. The effects of **inhibitor** concentration, temperature, and the extent of dilution on the achievement of a steady state equilibrium and the subsequent level and rate of recovery of brain cholinesterase activity were investigated. A similar procedure for reactivation of carbamate-inhibited plasma cholinesterase activity involved the removal of excess carbamate from a small sample volume (< 400 microliters). Both methods begin by **measuring cholinesterase activity** immediately following dilution and involve an incubation period during which conditions for spontaneous reactivation of the inhibited enzymes are maximized. Both assays are suitable for large-scale, rapid use and appear able to restore inhibited cholinesterase activity to levels closely approximating that of control values for each species tested. These methods will not only maximize the usefulness of cholinesterases in monitoring carbamate pesticide exposure but should prove to be extremely useful tools in the forensic assessment of carbamate exposure in human and wildlife pesticide incidents.

DUPLICATE 9

L25 ANSWER 25 OF 65 MEDLINE
ACCESSION NUMBER: 93345089 MEDLINE
DOCUMENT NUMBER: 93345089 PubMed ID: 8343985
TITLE: Rapid potentiometric determination of cholinesterases in plasma and red cells: application to eptastigmine monitoring.

Search completed by David Schreiber 308-4292

Gui [illegible], S

AUTHOR: Cazzola E; Lattuada N; Zocca L; Radice D; Luciana M; Imbimbo B P; Arteri A; Mosca A

CORPORATE SOURCE: Dipartimento di Scienze e Tecnologie Biomediche, Universita degli Studi, Milano, Italy.

SOURCE: CHEMICO-BIOLOGICAL INTERACTIONS, (1993 Jun) 87 (1-3) 265-8. Journal code: 1227276. ISSN: 0009-2797.

PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199309
ENTRY DATE: Entered STN: 19930924
Last Updated on STN: 19930924
Entered Medline: 19930903

AB Eptastigmine (MF 201) is a new physostigmine derivative with potent **inhibitory** activity on ch linesterases. Here we present a new potentiometric **cholinesterase activity assay** suitable for MF 201 monit rin:. The analysis is performed on a differential pH system and has the following characteristics: (a) within-run precision: C.V. 2. % (plasma cholinesterase), 1.8% (red cell cholinesterase); b) between-run precision: C.V. 4.0 (plasma cholinesterase), 6-70 U/g Hb (red cell cholinesterase); (c) linearity: 1-10 kU/l (plasma cholinesterase), 6-70 U/g Hb (red cell cholinesterase); (d) comparison with a reference method (i.e., HITACHI 737 Boerhunger Mannheim, Italy): y = 0.785x - 0.07; n = 37; r = 0.998. The assay has been applied to the determination of plasma and red cell cholinesterase activity in volunteers over 60 years of age treated with a single oral dose of 30 mg eptastigmine. We found that red cell cholinesterase is selectively inhibited after MF 201 administration with the following **kinetics** (time, % of inhibition, mean +/- S.E., n = 6): 0 h, 0; 1 h, 1[illegible] +/- 4.6; 2 h, 24 +/- 4; 4 h, 2[illegible] +/- 4.4; 12 h, 14 +/- 3. Eptastigmine plasma levels were also determined by a HPLC method: maximum concentration was found one hour after drug administration.

L25 ANSWER 26 OF 63 MEDLINE DUPLICATE 10
ACCESSION NUMBER: 94160095 MEDLINE
DOCUMENT NUMBER: 94160095 PubMed ID: 8115629
TITLE: Dengue in the south-eastern region of Brazil: historical analysis and epidemiology.

AUTHOR: Serufo J C; Souza A M; Tavares V A; Jammal M C; Silva J G
CORPORATE SOURCE: Virology Service, Ezequiel Dias Foundation, Belo Horizonte, MG, Brazil.

SOURCE: REVISTA DE SAUDE PUBLICA, (1993 Jun) 27 (3) 157-67. Journal code: 0136043. ISSN: 0034-8910.

PUB. COUNTRY: Brazil
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199405
ENTRY DATE: Entered STN: 19940406
Last Updated on STN: 19940406
Entered Medline: 19940329

AB The aim of the study is an historical analysis of the work undertaken by the Public Health organizations dedicated to the combat of the Aedes aegypti, as well as an epidemiological study of persons with unexplained fever, with a view to evaluating the occurrence of dengue within the population. The Mac-Elisa, Mic-Elisa, hemagglutination **inhibition**, isolation and typage tests were used. Organophosphate intoxication in agricultural workers was also assessed by **measuring concentrations** of seric **cholinesterase**. A sera

Search completed by David Schreiber 308-4292

samples of 2,[illegible] were collected in 23 towns, and the type 1 dengue virus was detected in 17 towns and autochthony was confirmed in 12 of them. The cholinesterase was measured in 2,391 sera samples of which [illegible] cases had abnormal levels. Poisoning was confirmed in 5 cases. Results reveal an epidemic the gravity of which was not officially know. The relationship between levels of IgM and IgG antibodies indicates the outbreak tendency. The widespread distribution of the vector is troubling because of the possibility of the urbanization of wild yellow fever, whereas the absence of A. aegypti in 2 towns with autochthony suggests the existence of another vector. Since there is no vaccine against dengue, the combat of the vector is the most efficient measure for preventing outbreaks. The eradication of the vector depends on government decisions which depend, for their execution, on the organization of the Health System and the propagation of information concerning the prevention of the disease using all possible means because short and long term results depend on the education and the active participation of the entire population.

DUPLICATE 11

L25 ANSWER 27 OF 63 MEDLINE
ACCESSION NUMBER: 93260733 MEDLINE
DOCUMENT NUMBER: 93260733 PubMed ID: 8492365
TITLE: A multiyear study of blood cholinesterase activity in urban pesticide applicators.
AUTHOR: Geary R A; Eaton J; Gilmore E; North B; Singell J
CORPORATE SOURCE: ChemLawn Clinical Laboratory, Trugreen-ChemLawn, Delaware, OH 43015-3863.
SOURCE: JOURNAL OF TOXICOLOGY AND ENVIRONMENTAL HEALTH, (1993 May) 39 (1) 11-25.
Journal code: 7513622. ISSN: 0098-4108.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199306
ENTRY DATE: Entered STN: 19930625
Last Updated on STN: 19930625
Entered Medline: 19930617

AB This article is a review of blood cholinesterase activity in a cohort of urban pesticide applicators ranging from 1660 to over 3800 workers. During the period 1981-1991, 308, 788 blood **samples** were taken for **measurement** of **cholinesterase activity** with an average of 6 **samples** per year from each worker. A total of 150 workers or 0.44 % of the cohort was removed from exposure to cholinesterase-**inhibiting** insecticides because of decreased cholinesterase activity. No worker required treatment for signs of cholinesterase **inhibition**.

DUPLICATE 12

L25 ANSWER 28 OF 63 MEDLINE
ACCESSION NUMBER: 92216457 MEDLINE
DOCUMENT NUMBER: 92216457 PubMed ID: 1525715
TITLE: Mechanism of inhibition of cholinesterases by huperzine A.
AUTHOR: Ashani Y; Peggins J O 3rd; **Doctor B P**
CORPORATE SOURCE: Walter Reed Army Institute of Research, Washington DC 20307.
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1992 Apr 30) 184 (2) 719-26.
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

Search completed by David Schreiber 308-4292

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199206
ENTRY DATE: Entered STN: 19920619
Last Updated on STN: 19970203
Entered Medline: 19920602

AB Huperzine A, an alkaloid isolated from Huperzia serrata was found to reversibly inhibit acetylcholinesterases (EC 3.1.1.7) and butyrylcholinesterases (EC 3.1.1.8) with on- and off-rates that depend on both the type and the source of enzyme. Long-term incubation of high **concentrations** of purified **cholinesterases** (1-8 microM) with huperzine A did not show any chemical modification of huperzine A. A low dissociation constant KI was obtained for mammalian acetylcholinesterase-huperzine (20-40 nM) compared to mammalian butyrylcholinesterase-huperzine (20-10 microM). This indicates that the thermodynamic stability of huperzine-cholinesterase complex may depend on the number and type of aromatic amino acid residues in the catalytic pocket region of the cholinesterase molecule.

DUPLICATE 13

L25 ANSWER 29 OF 63 MEDLINE
ACCESSION NUMBER: 92264775 MEDLINE
DOCUMENT NUMBER: 92264775 PubMed ID: 1375016
TITLE: Urinary excretion of diethylphosphorus metabolites in persons poisoned by quinalphos or chlorpyrifos.
AUTHOR: Vasilic Z; Drevenkar V; Rumenjak V; Stengl B; Frobe Z
CORPORATE SOURCE: Institute for Medical Research and Occupational Health, University of Zagreb, Croatia.
SOURCE: ARCHIVES OF ENVIRONMENTAL CONTAMINATION AND TOXICOLOGY, (1992 May) 22 (4) 441-7.
Journal code: 0357345. ISSN: 0090-4341.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; JOURNAL ARTICLE
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199206
ENTRY DATE: Entered STN: 19920626
Last Updated on STN: 19960130
Entered Medline: 19920616

AB The urinary excretion rates of diethyl phosphate and diethyl phosphorothioate and changes in blood cholinesterase activities were studied in fifteen persons self-poisoned either by the organophosphorus pesticide quinalphos (twelve persons) or by chlorpyrifos (three persons). The organophosphate poisoning was always indicated by a significant depression of serum and/or red blood cell cholinesterase activities. The return of serum cholinesterase activity in the range of referent values took more than 30 days and had a different course in different persons. The most rapid increase in red blood cell acetylcholinesterase activity was noted within 24 h after the first treatment with oximes Pralidoxime and/or HI-6. None of the spot urine samples, collected daily after admission of persons to hospital, contained measurable quantities of the parent pesticide. There was no correlation between the maximum concentration of total urinary diethylphosphorus metabolites normalized to creatinine and the initial **inhibition** of blood **cholinesterase activities measured** in **samples** collected on the day of admission to hospital. The excretion of metabolites followed the kinetics of a biphasic reaction. The half-time of urinary metabolites concentration decrease in the fast excretion phase in quinalphos poisoned persons was 5.5-14.2 h (eight persons) and 28.8-53.6 h (four persons) and in chlorpyrifos poisoned

persons ...-... h. The half-time for the slow excretion phase ranged from 66.8 to 127.9 h in all persons and for both compounds. For a given person, the rates of excretion of diethyl phosphate and diethyl phosphorothioate were about the same. However, in quinalphos poisoned persons the proportions of single metabolites in total diethylphosphorus metabolites varied with the initial maximum concentration of total metabolites.(ABSTRACT TRUNCATED AT 250 WORDS)

L25 ANSWER 30 OF 63 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1991:604724 HCAPLUS
DOCUMENT NUMBER: 115:204724
TITLE: Induction by some protein kinase **inhibitors** of differentiation of a mouse megakaryoblastic cell line established by coinfection with Abelson murine leukemia virus and recombinant SV40 retrovirus
AUTHOR(S): Honma, Yoshio; Okabe-Kado, Junko; Kasukabe, Takashi; Hozumi, Motoo; Kajigaya, Sachiko; Suda, Toshio; Miura, Yasusada
CORPORATE SOURCE: Dep. Chemother., Saitama Cancer Cent. Res. Inst., Ina, 362, Japan
SOURCE: Cancer Research (1991), 51(17), 4649-55
CODEN: CNREA8; ISSN: 0008-5472
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Mouse C1 line cells are megakaryoblastic cells established by coinfection of Abelson murine leukemia virus and recombinant simian virus 40. This study examd. the effects of various compds. on growth and differentiation of these cells. Megakaryocytic differentiation of C1 cells was not induced by cytokines that stimulate megakaryocyte maturation of normal progenitor cells, such as interleukin 3 and 6 and granulocyte-macrophage colony-stimulating factor. However, the cells were induced to differentiate into megakaryocytes by treatment with some protein kinase **inhibitors**. The **inhibition** of v-abl tyrosine kinase activity preceded induction of differentiation of the cells treated with tyrosine kinase **inhibitors** such as genistein, herbimycin A, and erbstatin. Treatment of C1 cells with a v-abl antisense oligomer **inhibited** their proliferation and induced acetyl**cholinesterase activity**, a typical marker of megakaryocytic **differentiation**. These results suggest that **inhibition** of v-abl function is assocd. with induction of megakaryocytic differentiation of C1 cells. Among the compds. tested, 1-(5-isoquinolinylsulfonyl)-2-methylpiperazine (H-7), a potent **inhibitor** of cyclic nucleotide-dependent and Ca2+-phospholipid-dependent (protein kinase C) protein kinases, was the most potent inducer of differentiation of C1 cells. However, the differentiation-inducing effect of H-7 was unlikely to be mediated through **inhibition** of protein kinase C or cyclic nucleotide-dependent kinases, because other types of **inhibitors** of these kinases were not effective, and a protein kinase activator (phorbol ester) induced differentiation of C1 cells. Moreover, neither v-abl mRNA expression nor v-abl kinase activity in C1 cells was affected by treatment with H-7. These findings indicate that induction of megakaryocytic differentiation by H-7 is not related to **inhibition** of v-abl kinase, but rather to some novel function of H-7.

L25 ANSWER 31 OF 63 SCISEARCH COPYRIGHT 2003 ISI (R)
ACCESSION NUMBER: 91:404295 SCISEARCH
THE GENUINE ARTICLE: FW559
TITLE: QUANTIFICATION AND PHENOTYPING OF SERUM-CHOLINESTERASE BY

Sue Gordon, 308-4292

ENZYME ANTIGEN IMMUNOASSAY - METHODOLOGICAL ASPECTS AND CLINICAL APPLICABILITY

AUTHOR: HANSAARD J (Reprint); WHITTAKER M; LOFT A G K; NORGAARD-PEDERSEN B

CORPORATE SOURCE: SONDERBORG HOSP, DEPT CLIN CHEM, DK-6400 SONDERBORG, DENMARK; POLYTECH S W, DEPT ENVIRONM SCI, PLYMOUTH, ENGLAND; STATENS SERUM INST, DEPT CLIN BIOCHEM, DK-2300 COPENHAGEN, DENMARK

COUNTRY OF AUTHOR: DENMARK; ENGLAND

SOURCE: SCANDINAVIAN JOURNAL OF CLINICAL & LABORATORY INVESTIGATION, 1991 Vol. 51, No. 4, pp. 349-358.

DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: ENGLISH
REFERENCE COUNT: 33

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB An enzyme antigen immunoassay for a specific determination of serum cholinesterase is described. Polyclonal and monoclonal antibodies against cholinesterase have been used. Hydrophobic binding of the specific antibody to a microtitre plate was followed by incubation with the **samples**, and the **activity** of the bound **cholinesterase** was **assayed** by the Ellman method. The procedure has been optimized and characterized, with respect to antigen specificity, and the applicability of the assay for cholinesterase phenotyping is demonstrated. The cholinesterase activities, dibucaine-, acoline-, fluoride- and urea numbers were comparable with established reference values. The high sensitivity and specificity of the assay has been used for determination of cholinesterase in amniotic and cerebrospinal fluids, and its applicability in clinical medicine is indicated.

L 5 ANSWER 32 OF 63 MEDLINE DUPLICATE 14

ACCESSION NUMBER: 89236767 MEDLINE
DOCUMENT NUMBER: 89236767 PubMed ID: 2738837

TITLE: Binary antidotes for organophosphate poisoning: aprophen analogues that are both antimuscarinics and carbamates.

AUTHOR: Leader H; Shepkal F M; Payne T S; Padilla F N; **Doctor B P; Gordon R K;** Chiang P K

CORPORATE SOURCE: Department of Applied Biochemistry, Walter Reed Army Institute of Research, Washington, D.C. 20307-5100.

SOURCE: JOURNAL OF MEDICINAL CHEMISTRY, (1989 Jul) 32 (7) 1522-8. Journal code: 9716531. ISSN: 0022-2623.

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198908
ENTRY DATE: Entered STN: 19900309
Last Updated on STN: 19970205
Entered Medline: 19890804

AB Prophylaxis against organophosphate poisoning can be achieved by pretreatment with physostigmine or pyridostigmine, which are carbamates, and aprophen, which is an anticholinergic agent. Thus, a series of aprophen analogues was synthesized with carbamyl substitutions on the phenyl rings (carbaphens). The rationale behind this design is that such compounds might exhibit most of the therapeutic characteristics of aprophen, as well as the ability to protect prophylactically by chemically masking cholinesterase enzymes. Compounds 4 (dimethylhydroxycarbaphen), 15 (dimethylcarbaphen), and 16 (monomethylcarbaphen) were found to inactivate

human butyrylcholinesterase in a time-dependent manner with potencies similar to those of physostigmine or pyridostigmine, and the latter two exhibited almost the same antimuscarinic profile as aprophen. In contrast to the potent inactivation of butyrylcholinesterase by these compounds, marginal inactivation of acetylcholinesterase activity was observed, and only at much higher drug concentrations. The noncarbamylated analogues had no effect on the **activity** of either **cholinesterase**. The carbaphen compounds are hence prototype drugs that can interact with either muscarinic receptors or butyrylcholinesterase. Furthermore, these compounds are prodrugs, since after carbamylation of the cholinesterase, the tertiary drug 14 (hydroxyaprophen) is a potent antimuscarinic itself.

L25 ANSWER 33 OF 63 MEDLINE DUPLICATE 15
ACCESSION NUMBER: 88266183 MEDLINE
DOCUMENT NUMBER: 88266183 PubMed ID: 3291446
TITLE: A **competitive** inhibition **enzyme** immunoassay for detection and quantification of organophosphorus compounds.
AUTHOR: Schmidt P; Kuhlmann R; Losch U
CORPORATE SOURCE: Institut fur Physiologie, Physiologische Chemie und Ernahrungsphysiologie, Tierarztliche Fakultat, Universitat Munchen, Bundesrepublik Deutschland.
SOURCE: ZEITSCHRIFT FUR NATURFORSCHUNG. SECTION C. JOURNAL OF BIOSCIENCES, (1988 Mar-Apr) 43 (3-4) 167-72.
Journal code: [illegible]. ISSN: 0341-0382.
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198809
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 20000303
Entered Medline: 19880811

AB A sensitive and specific method for detection and quantification of methyl phosphonic acid, p-aminophenyl 1,2,2-trimethyl-propyl diester (MATP) as a model substance for organophosphorus compounds is described. Different procedures for coupling the haptenic group for immunization, purification and immobilization allowed the detection of hapten-specific antibodies. The **competitive** inhibition **enzyme** immunoassay (CIEIA), using purified chicken and rabbit IgG-antibodies, was able to detect MATP-concentrations as low as 10(-10) mol/l. Based upon our results, we postulate that the CIEIA represents a good alternative to the customary diagnosis of organophosphate intoxications, **measuring** blood **cholinesterase activity**.

L25 ANSWER 34 OF 63 MEDLINE
ACCESSION NUMBER: 87238386 MEDLINE
DOCUMENT NUMBER: 87238386 PubMed ID: 3591648
TITLE: Cumulative toxicity potential of methomyl aerosol by repeated inhalation.
AUTHOR: Tanaka I; Igisu H; Haratake J; Cho S; Mori K; Fujishiro K; Inoue N; Horie A; Akiyama T
SOURCE: AMERICAN INDUSTRIAL HYGIENE ASSOCIATION JOURNAL, (1987 Apr) 48 (4) 330-4.
Journal code: 0371160. ISSN: 0002-8894.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals

Search completed by David Schreiber 308-4292

Aug [illegible], [illegible]

ENTRY MONTH: [illegible]
ENTRY DATE: Entered STN: 19900306
Last Updated on STN: 19970203
Entered Medline: 19870626

AB There are few investigations concerning the cumulative toxicity of agricultural chemicals by repeated inhalation. In this study, Wistar male rats were exposed to methomyl powder (mass median aerodynamic diameter, 4.4 microns) for a single 4-hr exposure, or for 4 hr/day, 5 days/week for 3 months. The average exposure concentrations were controlled at 9.9 mg/m3 for the single exposure and at 14.5 mg/m3 for repeated exposures by a dust generator consisting of a continuous fluidized bed with an overflow pipe and a screw feeder. After the repeated exposures, plasma and red cell **cholinesterase** activities, and lipid **concentrations** of the rat lungs were **measured** and histopathological examinations were performed. There was no evidence of cumulative effects on the red cell cholinesterase activity, histopathological changes and lipid concentration in 3-month repeated inhalation.

L25 ANSWER 35 OF 63 MEDLINE DUPLICATE 16
ACCESSION NUMBER: 85122396 MEDLINE
DOCUMENT NUMBER: 85122396 PubMed ID: 3970830
TITLE: Effect of a mixture of pyridostigmine and atropine on forced expiratory volume (FEV1), and serum cholinesterase activity in normal subjects.
AUTHOR: Feldt-Rasmussen B; Gefke P; Mosbech H; Hanel H K
SOURCE: BRITISH JOURNAL OF ANAESTHESIA, (1985 Feb) 57 (2) 204-7.
Journal code: 1372541. ISSN: 0007-0912.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198504
ENTRY DATE: Entered STN: 19900306
Last Updated on STN: 19970203
Entered Medline: 19850415

AB Pyridostigmine 0.143 mg kg-1 (maximum 10 mg) and atropine 0.0143 mg kg-1 (maximum 1 mg) were administered i.v. to six healthy male volunteers. Peripheral venous blood **samples** were drawn for **measurement** of serum **cholinesterase activity**. Maximum **inhibition** of the enzyme was found 5 min after injection with a decrease to 17 +/- 9% (mean +/- SEM) of the original activity. Forced expiratory volume in the first 1s (FEV1) was measured at fixed time intervals for 90 min. No decrease in FEV1 was observed; on the contrary, there was a small increase. We conclude that atropine effectively antagonizes the muscarinic side-effects of pyridostigmine on bronchial smooth muscle tone and bronchial secretions, when administered in clinical doses to normal human subjects.

L25 ANSWER 36 OF 63 MEDLINE DUPLICATE 17
ACCESSION NUMBER: [illegible] MEDLINE
DOCUMENT NUMBER: [illegible] PubMed ID: 6492454
TITLE: Serum **cholinesterase activity** in non-alcoholic fatty liver. Effect of obesity on the activity and role of its **measurement** in the **differential** diagnosis in chronic hepatitis.
AUTHOR: Nomura F; Ishii K; Koen H; Ohtsuki T; Kohno K; Saitoh M; Nakayama T; Hatano H; Mishima A; Hiyama Y; +
SOURCE: NIPPON SHOKAKIBYO GAKKAI ZASSHI. JAPANESE JOURNAL OF GASTROENTEROLOGY, (1984 Jul) 81 (7) 1569-75.

Search completed by David Schreiber 305-4292

Journal code: [illegible]. ISSN: [illegible].
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199412
ENTRY DATE: Entered STN: 19900320
Last Updated on STN: 19900320
Entered Medline: 19941219

L25 ANSWER 37 OF 65 MEDLINE
ACCESSION NUMBER: 84209532 MEDLINE
DOCUMENT NUMBER: 84209532 PubMed ID: 6724200
TITLE: Effects of inhaled hexamethylene diisocyanate (HDI) on guinea pig cholinesterases.
AUTHOR: Karol M H; Hansen G A; Brown W E
CONTRACT NUMBER: ES01572 (NIEHS)
OH00865 (NIOSH)
SOURCE: FUNDAMENTAL AND APPLIED TOXICOLOGY, (1984 Apr) 4 (2 Pt 1) 284-7.
Journal code: 8100838. ISSN: 0272-0590.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198407
ENTRY DATE: Entered STN: 19900220
Last Updated on STN: 19970203
Entered Medline: 19840702

AB Hexamethylene diisocyanate, HDI, a starting material in the production of many polyurethane products, was found to **inhibit** stoichiometrically mammalian and electric eel cholinesterases in an in vivo system (W. E. Brown, A. E. Green, M. H. Karol, and Y. Alarie , 1982, Toxicol . Appl. Pharmacol. 62, 45-52). The current study examined in vivo effects on guinea pig cholinesterases resulting from inhalation of HDI. Guinea pigs were exposed to atmospheres of 0.5, 1.8, or 4.0 ppm HDI (ceiling value = 0.02 ppm) for up to 6 hr. Blood samples were drawn prior to exposure and at specified times during exposure. No **inhibition** of serum cholinesterase was detected following exposure to 0.5 ppm HDI for 6 hr, to 1.8 ppm HDI for 2 hr, or to 4.0 ppm HDI for 3 hr. Similarly, no **inhibition** was detected when erythrocytes from each blood **sample** were **assayed** for acetylcholinesterase **activity**. Last, animals were sacrificed and **cholinesterase** activity determined in bronchial lavage fluid. Enzyme levels of HDI-exposed animals were not significantly different (P greater than 0.05) from those of control animals exposed to water vapor. In conclusion, although in vitro experiments had demonstrated potent anticholinesterase activity by HDI, in vivo inhalation exposure of guinea pigs to HDI at concentrations 25-200 times above the recommended (ACGIH) ceiling value did not produce measurable **inhibition** of cholinesterase activity.

L25 ANSWER 38 OF 65 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1985:137815 BIOSIS
DOCUMENT NUMBER: BA79:37811
TITLE: OBIDOXIME REACTIVATION OF ORGANOPHOSPHATE-**INHIBITED** CHOLINESTERASE ACTIVITY IN PIGS.
AUTHOR(S): SVED-HANSEN N; FRAUI I
CORPORATE SOURCE: DEP. PHARMACOLOGY TOXICOLOGY, ROYAL VET. AGRIC. UNIV.,

Search completed by David Schreiber 308-4292

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SOURCE: ACTA VET SCAND, (1984) 25 (1), 80-95.
CODEN: AVSCA7. ISSN: 0044-605X.

FILE SEGMENT: BA; OLD

LANGUAGE: English

AB Ability of obidoxime to reactivate [insecticide] organophosphate-**inhibited** cholinesterases was studied in pigs treated with either trichlorfon, DDVP or coumaphos. In 6 pigs **cholinesterase activity** was **measured** in blood **samples** before and after in vitro reactivation with obidoxime. Three pigs were treated with obidoxime ? h after administration of the organophosphates to study the possibility of in vivo reactivation. A close correlation was shown between the ability of obidoxime to reactivate the **inhibited** cholinesterases in vitro and in vivo. There was a marked difference in the possibility of reactivation between the 3 organophosphates. No reactivation was possible after treatment with DDVP, while reactivation could be achieved for at least ? h after administration of trichlorfon. After coumaphos treatment reactivation with obidoxime was possible for more than 24 h.

L25 ANSWER 39 OF 63 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 18

ACCESSION NUMBER: 1983:4?1349 HCAPLUS

DOCUMENT NUMBER: 99:5059?

TITLE: Specific **inhibitors** and substrates studies on the cholinesterases of Fasciola gigantica from sheep and goats

AUTHOR(S): Durrani, M. S.; Nawaz, M.; Chaudhry, N. I.

CORPORATE SOURCE: Fac. Vet. Sci., Univ. Agric., Faisalabad, Pak.

SOURCE: Cellular and Molecular Biology (Oxford) (1983), 29(1), ?-52
CODEN: CMBID4; ISSN: 0145-5680

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Specific **inhibitor** and substrate studies were conducted to det. and **differentiate** specific and nonspecific **cholinesterase activities** in the whole homogenates of F. gigantica obtained from sheep and goats. The **inhibitors** used were eserine, 1,5-bis(4-allyldimethylammoniumphenyl)pentan-3-one diiodide, tetraisopropyl pyrophosphoramide, octamethyl pyrophosphoramide, and DFP. The substrates included chlorides of acetylcholine, acetylmethylcholine, butyrylcholine, and benzylcholine. The normal values for total cholinesterases in the trematodes from sheep and goats were, resp., 0.283 and 0.222 .mu.mol acetylthiocholine hydrolyzed/mg P/min at 37.degree. by 20% homogenates of whole parasites. The specific cholinesterase in the homogenates of the trematode from sheep and goats was 74.2 and 77.0% and nonspecific cholinesterase was 23.3 and 23.0%, resp.

L25 ANSWER 40 OF 63 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 19

ACCESSION NUMBER: 1983:50759 HCAPLUS

DOCUMENT NUMBER: 98:5075?

TITLE: Studies on specific **inhibitors** and substrates of cholinesterases of Fasciola gigantica from cattle and buffaloes

AUTHOR(S): Durrani, M. S.; Nawaz, Muhammad; Chaudhary, N. I.

CORPORATE SOURCE: Fac. Vet. Sci., Univ. Agric., Faisalabad, Pak.

SOURCE: Zentralblatt fuer Veterinaermedizin, Reihe B (1982), 29(8), 636-41
CODEN: ZVRBA2; ISSN: 0514-7166

DOCUMENT TYPE: Journal

Search completed by David Schreiber 308-4292

LANGUAGE: English

AB Studies with specific **inhibitors** and substrates were carried out in order to **differentiate** the specific and nonspecific **cholinesterase activity** of a homogenate of complete F. gigantica parasites from cattle and buffalo. The **inhibitors** used were eserine, 1,5-bis(4-allyldimethylammonium phenyl)pentane-3-one dibromide, tetraisopropyl pyrophosphoramide, octamethyl pyrophosphoramide, and diisopropyl fluorophosphate. The specific substrates were chlorides of acetylcholine, acetylmethylcholine, butyrylcholine, and benzylcholine. The normal values for total activity of cholinesterase in the trematodes of cattle and buffaloes had a mean value of 0.294 and 0.300 .mu.M turnover of hydrolyzed acetothiocholine in mM P/min. at 37.degree. by a 20 homogenate of complete parasites. The proportion of specific cholinesterases in the trematode homogenates of cattle and buffalo was 68 and 72 and of nonspecific cholinesterase 28 and 32 , resp.

L25 ANSWER 41 OF 65 MEDLINE DUPLICATE 20
ACCESSION NUMBER: 81210634 MEDLINE
DOCUMENT NUMBER: 81210634 PubMed ID: 7237776
TITLE: Automated discrete **kinetic** method for erythrocyte acetylcholinesterase and plasma cholinesterase.
AUTHOR: Lewis P J; Lowry P F; Gorpertz D
SOURCE: CLINICAL CHEMISTRY, (1981 Jun) 27 (6) 926-9.
Journal code: 04.1540. ISSN: 0009-9147.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198108
ENTRY DATE: Entered STN: 19900816
Last Updated on STN: 19970203
Entered Medline: 19810820

AB We describe an automated **kinetic** method for erythrocyte acetylcholinesterase (EC 3.1.1.7) and plasma cholinesterase (EC 3.1.1.8) based on Ellman's colorimetric method. Quinidine sulfate is used as an **inhibitor** of plasma cholinesterase during the measurement of erythrocyte acetylcholinesterase activity, obviating the need for washing the erythrocytes before lysis. Results by this method are compared with those obtained by the electrometric delta pH method of Michel. To emphasize the need for **measuring** both erythrocyte acetylcholinesterase and plasma **cholinesterase activity** in workers exposed to organophosphate pesticides, we present a study of serial activities of both enzymes in a person accidentally exposed to demeton-S-methyl.

L25 ANSWER 42 OF 65 MEDLINE DUPLICATE 21
ACCESSION NUMBER: 82090050 MEDLINE
DOCUMENT NUMBER: 82090050 PubMed ID: 7316565
TITLE: Ozone **inhibition** of tissue cholinesterase in guinea pigs.
AUTHOR: Gordon T; Taylor S F; Amdur M O
CONTRACT NUMBER: ES 01359-02 (NIEHS)
SOURCE: ARCHIVES OF ENVIRONMENTAL HEALTH, (1981 Nov-Dec) 36 (6) 264-6.
Journal code: 0312627. ISSN: 0003-9896.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

Search completed by David Schreiber 308-4292

[illegible]

ENTRY MONTH: [illegible]
ENTRY DATE: Entered STN: 1990031[illegible]
Last Updated on STN: 19970203
Entered Medline: 1982022[illegible]

AB This study sought to determine if ozone at levels known to induce bronchial hyperreactivity in guinea pigs would **inhibit** tissue cholinesterase activity. Male, Hartley guinea pigs were exposed to filtered air, 0.1 ppm ozone, or 0.8 ppm ozone for 1 hr. Two hours after exposure, brain, lung, and diaphragm tissue **samples** were frozen for **assay** of **cholinesterase activity**. Brain **cholinesterase activity** was only minimally **inhibited** in either ozone exposure group. Both levels of ozone significantly **inhibited** lung cholinesterase activity compared to control animals' activity: a 17[illegible] decrease in activity in the 0.1 ppm ozone group (P less than .05) and a 1[illegible] decrease in the 0.8 ppm ozone group (P less than .05). Ozone at 0.8 ppm also **inhibited** activity in the diaphragm by 14 (P less than .[illegible]). To determine the degree of involvement of cholinesterase **inhibition** in bronchial hyperreactivity, parathion pretreated animals were challenged with histamine and the pulmonary function changes monitored. Parathion-treated animals had a peak resistance increase of 330 + - 1[illegible]4 (mean +.- SE), while the control vehicle animals' increase was 1[illegible]5 +/- 48[illegible]. The differences were not statistically significant, but show that cholinesterase **inhibition** may contribute to ozone-induced bronchial hyperreactivity.

L25 ANSWER 43 OF 63 MEDLINE DUPLICATE 22
ACCESSION NUMBER: 7722166[illegible] MEDLINE
DOCUMENT NUMBER: 7722166[illegible] PubMed ID: 880272
TITLE: A comparison of methods for **measuring** acetyl **cholinesterase activity** in blood **samples inhibited** by carbamates.
AUTHOR: French M C; Sellers [illegible]; Wilkinson R G
SOURCE: BIOCHEMICAL PHARMACOLOGY, (1977 Jul 1) 26 (13) 1263-6.
Journal code: [illegible]. ISSN: 0006-2952.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197709
ENTRY DATE: Entered STN: 19900314
Last Updated on STN: 19900314
Entered Medline: 19770825

L25 ANSWER 44 OF 63 MEDLINE
ACCESSION NUMBER: 7620[illegible] MEDLINE
DOCUMENT NUMBER: 7620[illegible] PubMed ID: [illegible]047
TITLE: The subcellular distribution and partial characterization of cholinesterase activities of canine platelets.
AUTHOR: Lovette K M; Chuang H Y; Mohammad A F; Mason R G
SOURCE: BIOCHIMICA ET BIOPHYSICA ACTA, (1976 Apr 23) 428 (2) 355-63.
Journal code: 0217513. ISSN: 0006-3002.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197608
ENTRY DATE: Entered STN: 19900313
Last Updated on STN: 19970203

Search completed by David Schreiber 308-4292

Entered Medline: 19761001

AB The multiple cholinesterase activities in canine platelets have been investigated. Platelets were homogenized by rapid decompression under nitrogen, glass tube/Teflon pestle, and glycerol lysis techniques. Rapid decompression under nitrogen technique was found to be the most efficient and gentle method for cell disruption. Homogenates were subfractionated using sodium diatrizoate density gradients. Marker enzyme assays and pulse labeling experiments with 5-hydroxyl[14C] tryptamine and [125I] thrombin on prepared subcellular fractions confirmed that the soluble, plasma membrane and the granule-1 fractions were all in reasonably pure form. Furthermore, labeling of the plasma membrane with [125I] thrombin is cited as the first successful attempt at attaining significantly bound marker for this structure. **Cholinesterase activity** distributions **measured** in these fractions indicated that about 80% of the activity was present in the plasma membrane, 50% in granule-1 and 5% in soluble fractions. **Kinetic** data of cholinesterase activities obtained from intact platelets, plasma membrane preparations and platelet release supernatants indicated that they are strikingly similar.

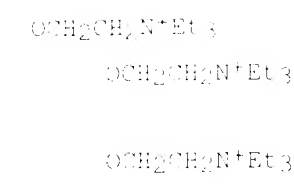
L25 ANSWER 45 OF 63 MEDLINE
ACCESSION NUMBER: 76233892 MEDLINE
DOCUMENT NUMBER: 76233892 PubMed ID: 947480
TITLE: Choline-esterase activity and choline uptake in intact nerve cell cultures.
AUTHOR: Massarelli R; Stefanovic V; Mandel P
SOURCE: BRAIN RESEARCH, (1976 Aug 6) 112 (1) 103-12.
Journal code: 0045503. ISSN: 0006-8993.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197610
ENTRY DATE: Entered STN: 19900313
Last Updated on STN: 19970203
Entered Medline: 19761001

AB Choline uptake and ecto-**cholinesterase activities** have been **measured** in intact astroblast and neuroblast cultures. The data show that choline uptake is dependent upon the ionic composition of the culture medium and is sensitive to metabolic **inhibitors**. However, the high concentrations of the **inhibitors** necessary for the inhibition of the uptake and some thermodynamic properties would suggest a facilitated transport rather than an active uphill process. Preincubation of the cultures with various **inhibitors** of cholinesterases shows no direct parallelism between inhibition of choline high affinity uptake (apparent Km approximately equal to 10-6 M) and inhibition of ecto-acetylcholinesterase (EC 3.1.1.7).

L25 ANSWER 46 OF 63 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1976:441046 HCAPLUS
DOCUMENT NUMBER: 85:41046
TITLE: Cholinesterase activity and the pattern of innervation in human skeletal muscles after administration of relaxant drugs
AUTHOR(S): Merhom, K.; Moustafa, Fatma A.
CORPORATE SOURCE: Fac. Med., Ain Shams Univ., Cairo, Egypt
SOURCE: Ain Shams Medical Journal (1976), 27(1), 53-5
CODEN: AIMJA9; ISSN: 0002-2144
DOCUMENT TYPE: Journal

Search completed by David Schreiber 308-4292

LANGUAGE: English
GI



AB Muscle relaxation of surgical patients with gallamine triethiodide (I) [65-29-2] (2 mg/kg) in connection with anesthesia increased the histochem. **detectable cholinesterase** [9001-08-5] **activity** in rectus muscle biopsy **samples**. In addn., I caused diffusion and expansion of the motor end plates, localized swellings of the intramuscular nerve fibers, and varicosities and arborization of subterminal fibers. Similar treatment of patients with suxamethonium [306-40-1], instead of I, caused **inhibition** and depletion of cholinesterase from the muscle end plates, together with shrinkage and vacuolation of acetylcholine vesicles.

L25 ANSWER 47 OF 63 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 23
ACCESSION NUMBER: 1974:560489 HCAPLUS
DOCUMENT NUMBER: 81:166914
TITLE: Ultrastructural localization of cholinesterase activity in the developing rat retina
AUTHOR(S): Spira, Arthur W.
CORPORATE SOURCE: Dev. Morphol. Sci., Univ. Calgary, Calgary, Can.
SOURCE: Journal of Histochemistry and Cytochemistry (1974), 22(9), 778-80
CODEN: JHCYAS; ISSN: 0022-1554
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Retina of rats from the 16th day of gestation to 10 weeks postnatal age were treated for the ultrastructural localization of cholinesterases according to the method of Lewis and Shute. The use of selective **inhibitors** served to **differentiate** between acetylcholinesterase and nonspecific **cholinesterase activities**. Nonspecific cholinesterase activity was marked in the rough endoplasmic reticulum of pigmented epithelium but only during the 1st 2 postnatal weeks. Acetylcholinesterase activity was prominent in the rough endoplasmic reticulum, nuclear envelope and Golgi app. of ganglion cells in fetal and mature retina; transiently, between processes in the outer plexiform layer and in the perikarya of some horizontal cells; and between processes in the inner plexiform layer coincident with the appearance of synapses, as well as in the mature retina. These localizations are suggestive of an assocn. between cholinesterases and early stages of photoreceptor segment formation and are consistent with a function in plexiform layer maturation and synaptic transmission in the inner plexiform layer.

L25 ANSWER 48 OF 63 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 24
ACCESSION NUMBER: 1973:414300 HCAPLUS
DOCUMENT NUMBER: 79:14400

Search completed by David Schreiber 308-4292

TITLE: Characterization of canine hepatic and renal esterases
AUTHOR(S): Ecobichon, D. J.
CORPORATE SOURCE: Dep. Pharmacol., Dalhousie Univ., Halifax, NS, Can.
SOURCE: Canadian Journal of Biochemistry (1973), 51(5), 506-13
CODEN: CJBIAE; ISSN: 0008-4018
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The esterases of canine liver and kidney were sepd. electrophoretically into 9 bands with identical migration patterns in both tissues. An addnl. pair of rapidly migrating anodic bands were obsd. in hepatic exts. Based on substrate specificity, the predominant tissue esterases were identified as nonspecific carboxylesterases (aliesterases). No **cholinesterase activity** was **detected** in the tissue exts. **Kinetic** characteristics detd. for the hepatic and renal esterases included optimal pH, Km values for esters of .alpha.-naphthyl and p-nitrophenol, and av. rates of hydrolysis of .alpha.-naphthyl acetate and p-naphthyl acetate and p-nitrophenyl acetate by the tissue exts. Inhibition studies revealed the presence of 2 types of esterase activity in each tissue; one type being sensitive to organophosphorus esters, the second being resistant. A study of preferential substrate hydrolysis in the presence of known characteristic activators and **inhibitors** of esterases revealed .apprx. 5% and 20% arylesterase activity in liver and kidney, resp. The presence of arylesterase activity in these tissues was confirmed by the hydrolysis of paraoxon.

L25 ANSWER 49 OF 63 EMBASE
ACCESSION NUMBER: 74014781 EMBASE
DOCUMENT NUMBER: 1974014781
TITLE: Effect of sample storage on human blood cholinesterase activity after **inhibition** by carbamates.
AUTHOR: Wilhelm K.; Reiner E.
CORPORATE SOURCE: Inst. Med. Res. Occupat. Hlth, Yugoslav Acad. Sci. Arts, Zagreb, Yugoslavia
SOURCE: Bulletin of the World Health Organization, (1973) 48/2 (235-238).
CODEN: BWHOA6
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
029 Clinical Biochemistry
025 Hematology
035 Occupational Health and Industrial Medicine
030 Pharmacology
LANGUAGE: English

AB During an operational field trial with propoxur it was observed that the **inhibition** of whole blood cholinesterase was greater when **samples** were stored before the **assay**. Since measurement of **cholinesterase activity** is not always possible immediately after sampling, the effects of different storage conditions were evaluated. Human blood cholinesterases were **inhibited** in vitro by methylcarbamates and stored at different pH values, temperatures, and sample dilutions. The results showed that the degree of cholinesterase **inhibition** does not change if samples are diluted 300 fold with buffer at pH 5, at 4.degree. C and the enzyme activity measured within 4 hr of dilution. These conditions of storage were equally satisfactory for each of the three methylcarbamates studied and are therefore likely to apply to other carbamates as well.

L25 ANSWER 50 OF 63 HCAPLUS

Search completed by David Schreiber 308-4292

ACCESSION NUMBER: 1971:137696 BIOSIS
DOCUMENT NUMBER: 71:137696
TITLE: Genetic regulation of plasma cholinesterase in man
AUTHOR(S): La Du, B. N.; Dewald, B.
CORPORATE SOURCE: Sch. Med., New York Univ., New York, NY, USA
SOURCE: Advances in Enzyme Regulation (1971), 9, 317-32
CODEN: AEZRA2; ISSN: 0065-2571
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Individual variation in response to succinylcholine has stimulated investigations on the variations and genetic control of serum cholinesterase in man. The level of **cholinesterase** varied from essentially no **detectable activity** to exceedingly high levels due to a no. of different genetic mutations. Qual. variations in the esterase were also inherited. The most common variant of the latter type was the atypical (dibucaine-resistant cholinesterase which differed from the normal esterase in its lower apparent affinity for choline ester substrates and for a no. of **inhibitors**. **Kinetic** expts. showed modification of both the anionic and esteratic sites of the atypical esterase. These changes may be due to a difference in the primary structure of the enzyme at 1 position which affects both sites of the active center of the enzyme. The modified **kinetic** properties of the atypical esterase were expressed in both the major component (C4) and the minor components (C1, C2, and C3) of the enzyme which was present in serum in multiple mol. forms. Component C4 (mol. wt. of .apprx.300,000) could be converted to component C3 by treatment with urea, and the latter transformed to a C1-like component by SH reagents. Both C1 components (native and derived) had mol. wts. of .apprx.80,000.

L25 ANSWER 51 OF 63 MEDLINE DUPLICATE 25
ACCESSION NUMBER: 71109676 MEDLINE
DOCUMENT NUMBER: 71109676 PubMed ID: 5100961
TITLE: A manual and automated procedure for measuring serum **cholinesterase activity** and identifying enzyme variants. **Differentiation** by means of Tris and phosphate buffers.
AUTHOR: Garry P J
SOURCE: CLINICAL CHEMISTRY, (1971 Mar) 17 (3) 192-8.
Journal code: 9421548. ISSN: 0009-9147.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197103
ENTRY DATE: Entered STN: 19900101
Last Updated on STN: 19900101
Entered Medline: 19710301

L25 ANSWER 52 OF 63 HCAPLUS COPYRIGHT 2005 ACS
ACCESSION NUMBER: 1968:503216 HCAPLUS
DOCUMENT NUMBER: 69:103216
TITLE: Acetyl- and pseudocholinesterase activities in sympathetic ganglia of rats
AUTHOR(S): Klingman, Gerda I.; Klingman, J. D.; Polisaczuk, Anna
CORPORATE SOURCE: Sch. of Pharm., State Univ. of New York, Buffalo, NY, USA
SOURCE: Journal of Neurochemistry (1968), 15(10), 1121-30
CODEN: JONHA9; ISSN: 0022-3042
DOCUMENT TYPE: Journal

Search completed by David Schreiber 308-4292

LANGUAGE: English

AB The quant. method of Ellman, et al., (1961) was adapted to a **differential assay** for the detn. of acetyl- (I) and pseudocholinesterase (II) activities of sympathetic ganglia of rats. The **activities** of the **cholinesterases** of superior cervical, stellate, and thoracic chain ganglia and of the abdominal ganglionic complexes in apposition to the superior mesenteric and celiac arteries (superior mesenteric, celiac, and cardiac ganglia) were measured. B.W.284C51 dibromide, 5 .times. 10-6M, and ethopropazine-HCl, 3.15 .times. 10-5M, were employed to inhibit selectively I and II, resp. Linearity was maintained with enzyme concns. corresponding to 0.12-0.5 mg. of ganglion (wet wt.)/incubation. Under the exptl. conditions of this assay, the rates of the reaction of ganglionic I and II were linear for time periods greater than those employed for calcn. the rates of hydrolysis in the homogenates of sympathetic ganglia. Several exptl. approaches were used to ascertain the specificity of the inhibitors and of the reaction. Of the total **cholinesterase activity** of sympathetic ganglia of rats, 55-63 was due to I and 31-39 to II. On the basis of the sp. enzyme activity, superior cervical, stellate, and superior mesenteric ganglia contained higher I and II activities than did thoracic chain, celiac, and cardiac (abdominal) ganglia. The sp. activity of I was similar in rat and cat superior cervical ganglia and sympathetic cervical trunks while the II activity of these 2 tissues was somewhat lower in cats than in rats.

L25 ANSWER 53 OF 65 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1968:116214 HCAPLUS
DOCUMENT NUMBER: 68:116214
TITLE: Tacrine **inhibition** of serum cholinesterase and prolonged succinylcholine action
AUTHOR(S): Benveniste, Daniel; Hemmingsen, Lars; Juul, Per
CORPORATE SOURCE: Central Hosp., Nykoebing, Den.
SOURCE: Acta Anaesthesiologica Scandinavica (1967), 11(3), 297-308
CODEN: AASCAS; ISSN: 0001-5172
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The percent inactivation of serum cholinesterase by tacrine was measured in 38 unanesthetized patients and in 62 anesthetized patients paralyzed by intermittent doses of 12.5 to 50 mg. succinylcholine. The dose of tacrine was 30 mg. administered i.m. in 15 patients or i.v. in 75 patients, preceded by atropine. The pharmacol. actions of tacrine on anesthetized patients were a prolongation of the neuromuscular action of succinylcholine and a redn. of the total amt. of succinylcholine needed. The incidence of post-operative muscle pain was only 5%. There were a few side effects, including increased tendency towards bradycardia and insignificant alterations in blood pressure. Respiratory insufficiency at the end of anesthesia occurred in 2 patients and a mild psychosis occurred in one patient 2 days postoperatively. Blood **samples** were withdrawn and **cholinesterase activity measured** by continuous titrn. technique. The mean value of serum cholinesterase activity in this series was 3.0 micromoles/ml./min. The mean degree of **inhibition** of serum cholinesterase by tacrine was low, 23% at 1 hr. after i.m. injection and 22% at 15 min. after i.v. injection. The **inhibition** decreases progressively, but more rapidly when tacrine is given i.v. Since this is in apparent disagreement with the clin. observations on tacrine administration, the effects of the diln. and substrate concn. on percent **inhibition** were investigated and showed that the **inhibition** by tacrine in vivo attained a much

Page [illegible]

higher value, [illegible], at 15 min. after injection. As succinylcholine is an anticholinesterase, it will apparently have the same effect on a homozygote with the atypical or silent gene receiving the succinylcholine simultaneously. 34 references.

L25 ANSWER 54 OF 63 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1968:56765 HCAPLUS
DOCUMENT NUMBER: 68:56765
TITLE: Electron-microscopic localization of cholinesterase in the nervous system
AUTHOR(S): Koelle, George B.
CORPORATE SOURCE: Univ. of Pennsylvania, Philadelphia, PA, USA
SOURCE: Biokhim. Punkts. Nervn. Sist., Mater. Mezhdunar. Simp. 1967), Meeting Date 1965, 185-8, discussion 189
CODEN: [illegible]THAB
DOCUMENT TYPE: Conference
LANGUAGE: Russian

AB Thiocholine was used as substrate for brain cholinesterase. The produced thiocholine phosphate reacted with Au(CN)2 and (NH4)2S. The colloidal AuS visualized the sites of enzyme activity. The diffusion of enzymes in electron microscopic slices was reduced by incubation in highly concd. buffers and Na2SO4. The specific acetylcholinesterase and nonspecific **cholinesterase activities** were **differentiated** by specific **inhibitors**, such as eserine or diisopropyl fluorophosphate. The acetylcholinesterase activity was localized in the terminal membrane of the axon and in the postsynaptic membrane. The nonspecific cholinesterase had similar distribution but its activity was low.

L25 ANSWER 55 OF 63 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1966:41656 HCAPLUS
DOCUMENT NUMBER: 65:41656
ORIGINAL REFERENCE NO.: 65:8317a-e
TITLE: The **kinetics** of cholinesterases measured fluorometrically
AUTHOR(S): Siegel, George J.; Lehrer, Gerard M.; Silides, Demetra
CORPORATE SOURCE: Div. of Neurochem., Mt. Sinai Hosp., New York, NY
SOURCE: J. Histochem. Cytochem. (1966), 14(6), 473-8
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A new simple sensitive method is described for the fluorometric **assay** of **cholinesterase activity** based on the hydrolysis of 1-naphthyl esters and the measurement of the fluorescence of 1-naphthol. This permits the study of the **kinetics** of cholinesterases and **inhibitors** with histochem. substances and permits assessment of the parameters of the enzyme reaction under conditions approximating those in the histochem. system. 1-Naphthylacetate is a substrate for acetylcholinesterase (I) and cholinesterase (II), while 1-naphthyl butyrate is selective for II. The application of the procedure to the study of inhibition by hydrolyzable as well as nonhydrolyzable nonelectrogenic **inhibitors** is demonstrated. Acetylcholine was found to be a mixed **inhibitor** of both I and II in this system. Edrophonium was found to be a more potent competitive **inhibitor** of I than either physostigmine or pyridostigmine, but a much weaker **inhibitor** of II than the latter 2. Ambenonium behaves as a noncompetitive **inhibitor** of II; it is at least 10,000 times more effective on I, and is 300 times more potent an **inhibitor** of I than is physostigmine. The use of edrophonium and ambenonium as selective **inhibitors** of I is

[illegible]

[illegible]

L25 ANSWER 56 OF 65 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1964:24558 HCAPLUS
DOCUMENT NUMBER: 60:24558
ORIGINAL REFERENCE NO.: 60:4397f-h,4398a-b
TITLE: **Cholinesterase activity** on a new compound of analogous structure to acetylcholine: dimethylaminooxyethyl acetate methiodide (L277) in comparison with dimethylaminopropyl acetate methiodide (L248)
AUTHOR(S): Schiatti, P.; Marilli, G.
CORPORATE SOURCE: Lepetit S.p.A., Milan
SOURCE: Boll. Soc. Ital. Biol. Sper. (1962), 38(24), 1823-6
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB Dimethylaminooxyethyl acetate methiodide (I) and dimethylaminopropyl acetate methiodide (II) were compared with acetylcholine (III) as substrates for cholinesterase (IV) and pseudocholinesterase (V). All 3 substrates were detd. by adding 1 ml. of soln. to 1 ml. of alk. hydroxylamine freshly prepd. by mixing equal vols. of 14% NaOH and 14% NH2OH.HCl. After 3 min. at room temp. 1.5N HCl (1 ml.) and 5% FeCl3.6H2O soln. in 0.1N HCl (2 ml.) were added and, after shaking well, the extinction was measured at 540 m.mu. against a reagent blank and converted to wt. of substrate by reference to a **standard curve**. IV was prepd. from guinea pig red blood cells according to Mentha, et al. (CA 41, 3152g) and V from guinea pig serum according to Strelitz (CA 38, 551[1]). Esterase activity was first detd approx. by incubation of 1 ml. of 0.1M substrate in Ringer's soln. with the enzyme prepn., for 20 min. at 30.degree. then detg. the substrate as above. Activity was then detd. manometrically in a Warburg app. by measuring the CO2 evolved in 20 min. at 30.degree. from 0.01M substrate. The inhibition induced by eserine was similarly measured by adding eserine sulfate to the substrate soln. to a final concn. of 5 .times.10-7M to 10-4M. The Ki was calcd. according to Lineweaver and Burk (CA 28, 3021[1]). Both IV and V hydrolyze I, II, and III. The Ki values (.times. 10-8M) were: for IV I 1.37, II 1.51, III (.7%; for V I 4.28, II 1.4%, III 1.1%. Concns. of eserine producing 50% inhibition of enzyme activity were: (.times. 10-8M): for IV I 2.5, II 2.1, III 8.4; for VI 1.1, II 0.9, III 1.4. These results show that the modification of the acetylcholine mol. produced by introducing an O atom between the methylene chain and the quaternary N has the same effect as lengthening the methylene chain by another CH2 group. Both types of cholinesterase have an equal affinity for I and II which is, however, less than but of the same order as that for III.

L25 ANSWER 57 OF 65 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1961:60335 HCAPLUS
DOCUMENT NUMBER: 55:60335
ORIGINAL REFERENCE NO.: 55:11577g-i,11578a
TITLE: The activity of specific and nonspecific cholinesterases in the development of the optic lobes of the chicken
AUTHOR(S): Filogamo, Guido
CORPORATE SOURCE: Ist. anat. Turin, Italy
SOURCE: Arch. biol. (Liege) (1960), 71, 169-98
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB Cf. Acta Anat., 35, 349(1958). The appearance and distribution of the enzymes in the optic cup of the chick embryo were investigated by means of

the technique of Koelle [illegible]. Pharmacol. Exptl. Therapeut. [illegible]. Acetylcholinesterase (I) and nonspecific **cholinesterase** (II) **activities** were **differentiated** by the use of acetylthiocholine and butyrylthiocholine as substrates and Mipafox as an **inhibitor** of II. I activity is present in the neuroblasts of the mesencephalic vesicle as early as stage 20, and in these neurons it is strictly localized in the perikaryon up to stage 40 (14th day of incubation). Between stages 41 and 45 it is present in the plexiform layers and the pericellular plexuses. It is consistently absent in the 5th Cajal layer and the pericellular plexuses of the 13th layer, as well as in the optic fiber layers, the deep white matter, and ependyma. After section of the optic fibers, I activity becomes neg. in the retinal layer. No correlation could be found between the appearance of I and synaptic development. II activity is diffusely present in the optic vesicle from the earliest stage studied (20). After stage 36 the activity is diminished, although it rises in the fibrous layer at stage 43. Enucleation of the eye from the newborn chick results in the disappearance of II from the optic layer.

L25 ANSWER 58 OF 63 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1960:33946 HCAPLUS
DOCUMENT NUMBER: 54:33964
ORIGINAL REFERENCE NO.: 54:7854h-i
TITLE: Enzymic properties of cholinesterases in subcellular fractions from rat brain
AUTHOR(S): Holmstedt, B.; Toschi, G.
CORPORATE SOURCE: Karolinska Inst., Stockholm
SOURCE: Acta Physiol. Scand. (1959), 47, 280-3
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB Mitochondria, microsomes, and a sol. fraction, prepd. from rat brain homogenate by **differential** centrifugation, were **assayed** for **cholinesterase** (I) **activity** with different substrates. The activity of true I is higher in mitochondria and microsomes than in the whole homogenate, whereas pseudo I activity is more concd. in the sol. fraction. The assocn. of true I with membrane-rich fractions is stressed.

L25 ANSWER 59 OF 63 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1960:7605 HCAPLUS
DOCUMENT NUMBER: 54:7605
ORIGINAL REFERENCE NO.: 54:1635d-e
TITLE: **Differentiation** of the **cholinesterase activity** of biological materials of various origin by means of **inhibitors**
AUTHOR(S): Ferrari, W.; Gessa, G.; Vargiu, L.
CORPORATE SOURCE: Univ. Cagliari, Italy
SOURCE: Arch. ital. sci. farmacol. (1959), 9, 153-6
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB A table is given of the eserine, eucupine, CT 3318 [bis(piperidinomethylcoumarin-5-yl) ketone bis(iodomethylate)] (I), and Mintacol (E 600) concns. which can **inhibit** by 50% , in vitro, the cholinesterase activity of the blood serum, brain, or muscle of various animals. On the basis of this behavior, the following cholinesterase types are pointed out: (1) eucupine-sensitive and I-resistant (human and horse blood serum), (2) eucupine-resistant and I-sensitive (horse, dog, rat, mouse pig, cat, rabbit and pig brain), and (3) both eucupine- and

I-resistant (dog, rat, guinea pig, chick, duck, and pigeon blood serum; chick, duck and pigeon brain; rat, guinea pig, and frog striated muscle).

L25 ANSWER 60 OF 63 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1958:88567 HCAPLUS
DOCUMENT NUMBER: 52:88567
ORIGINAL REFERENCE NO.: 52:15631i,15632a-c
TITLE: Potentiometric method for the determination of **cholinesterase activity**
AUTHOR(S): Goshev, A. I.
CORPORATE SOURCE: V. M. Bekhterev Sci. Research Inst Psychoneurol, Leningrad
SOURCE: Voprosy Med. Khim. (1958), 4, 149-54
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB The method described, which permits the detn. of **cholinesterase activity** in 0.1 g. of any tissue or 0.1 ml. of any biol. fluid, consists of measuring, by means of an Sb electrode, the changes in pH of a borate buffer contg. the material to be tested and acetylcholine. The Sb electrode (made of a pure Sb plate to which a Cu wire, enclosed in a glass tube, is soldered) is calibrated against a calibrated calomel electrode in borate buffer solns. The **standard curve** is prepd. by using a borate buffer at pH 8.5, dild. with CO_2-free water, to which AcOH in varying amts. has been added; a similar curve is prepd. for blank detns. from a 1:2 diln. of the buffer with addn. of AcOH. The dild. sample, enough NaOH to neutralize 1 ml. of acetylcholine soln., and 1 ml. of acetylcholine soln. are added to the dild. buffer and the mixt. is incubated at 38.degree.. The blank consists of the same mixt. to which 2 drops of physostigmine have been added. At the end of the incubation period (usually 30 min.) physostigmine is added to the test mixt. and the pH of both the blank and the test (in duplicate) is measured with the Sb electrode. The **cholinesterase activity** (expressed in micromoles AcOH) is calcd. from the formula: (A - B)N/t, where A equals micromoles AcOH in the test, B the micromoles AcOH in the blank, t the time of incubation, and N the diln. of the sample. Data are presented for the **activity** of **cholinesterase** in rabbit brain and human blood (whole blood, plasma, and erythrocytes).

L25 ANSWER 61 OF 63 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1956:32343 HCAPLUS
DOCUMENT NUMBER: 50:32343
ORIGINAL REFERENCE NO.: 50:6521i,6522a,6523a
TITLE: **Differentiation** of **cholinesterase activity** of biologic material of diverse origin. II. **Inhibition** due to bis(piperidinomethylcoumaran-5-yl)ketone (CT 3318)
AUTHOR(S): Paulesu, F.; Margiu, L.; Gibertoni, G.
SOURCE: Arch. intern. pharmacodynamie (1955), 104, 11-18
DOCUMENT TYPE: Journal
LANGUAGE: Italian

AB (CT 3318 (I) (C.A. 48, 3333c) is a highly active selective cholinesterase (II) **inhibitor**. Titration in vitro according to the modified method of Ferrari (C.A. 42, 5065e) on serums from man, horses, dogs, rabbits, rats, and chickens and on brain tissue from rabbits, guinea pigs, horses, dogs, and chickens shows that the **inhibitory** effect of I varies according to the origin of the material providing the active II. Based on the sensitivity of the enzymes towards eucupine (III), a selective **inhibitor** of pseudocholinesterase, and towards I, a new type of cholinesterase, resistant to I and III, may be present in the

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sera of rats and chickens and in chicken brain tissue.

L25 ANSWER 62 OF 63 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1949:50774 HCAPLUS
DOCUMENT NUMBER: 43:50774
ORIGINAL REFERENCE NO.: 43:9108h-f
TITLE: Critique and procedure for cholinesterase determinations in blood
AUTHOR(S): Schaefer, Hans; Maier, Erich
SOURCE: Biochem. Z. (1943), 319, 420-38
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB The hydrolysis of acetylcholine (ACh) in human blood under physiol. conditions, i.e., very small concns., is almost entirely due to cholinesterase of the erythrocytes and practically none to cholinesterase of the serum. Therefore, changes in serum cholinesterase values are physiologically without importance so long as the erythrocyte cholinesterase values are normal. It is important to bear clearly in mind that, wherever cholinesterase is diminished, the ACh liberated at any parasympathetic ending remains active for a longer than normal duration. As a result a vagotonia develops, or temporary predominant parasympathetic innervation. Of course, this hypothesis presupposes that the ACh measured is the ACh which is effective in the vegetative field upon which the parasympathetic acts. It always seemed more or less doubtful whether the serum cholinesterase represented such a reference. The motor end plate is definitely the place where ACh is liberated, as can be judged by its high local concn. It is not permissible thus to regard a decrease in serum cholinesterase as an indication of increased vagotonus. Besides, since the serum cholinesterase is presumably an unspecific pseudocholinesterase, its variations probably reflect changes in the compn. of protein fractions rather than those in the vegetative hormonal system. But neither does the detn. of erythrocyte cholinesterase reveal anything regarding the cholinergic transmission at the vegetative end organs. Certain **kinetic** constants must be **measured** to det. the **cholinesterase activity** of erythrocytes. This is done in the Warburg app. and from these detns. the relative cholinesterase concn. is calcd., as well as the mode of binding of ACh and cholinesterase, and finally the equil. constant of the **inhibitory** reaction between cholinesterase and ACh. The cholinesterase concn. attains a min. at about 50 years of age.

L25 ANSWER 63 OF 63 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1949:34513 HCAPLUS
DOCUMENT NUMBER: 43:34513
ORIGINAL REFERENCE NO.: 43:6272b-d
TITLE: New technique for the estimation of **cholinesterase activity** in blood serum
AUTHOR(S): Gal, I.
SOURCE: Ann. biol. clin. (Paris) (1943), 6, 383-5
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB Dil. protein solns. become opaque through the action of AcOH; the opacity is directly proportional to the amt. of AcOH. **Cholinesterase activity** (I) can be measured with an accuracy of 3-5 by use of this observation. A **standard curve** is prepd. by heating 0.3 ml. serum and 0.3 ml. milk dild. 1 to 10, adding 0.1 to 0.5 ml. 0.01 M AcOH and water to make 2.7 ml., and measuring the opalescence nephelometrically. To assay I, mix 0.3 ml. serum, 0.3 ml. dil. milk, 0.1

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ml. [illegible] M acetylcholine (II) and 1.1 ml. H_2O. Est. the opacity at 1 min. intervals and det. the time when half the II has been hydrolyzed. I is expressed as the reciprocal of this time, multiplied by 1000. Opacity produced by A + II must be instantaneous, since there is no further change in opacity after addn. of eserine. Serum shows no loss of I on refrigerated storage for 2-14 days.

Research completed by David Schreiber 308-4292